or condition by antagonizing the CCR1 receptor, and to their methods of preparation and use. A method of preparing crystalline I comprises (a) mixing I in a solvent mixture of methanol and methylene chloride, (b) distilling the mixture obtained to remove methanol, and (c) crystallizing the mix. in a solvent system comprising Et acetate.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l50 ibib fhitstr abs 2-
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

YOU HAVE REQUESTED DATA FROM 33 ANSWERS - CONTINUE? Y/(N):y

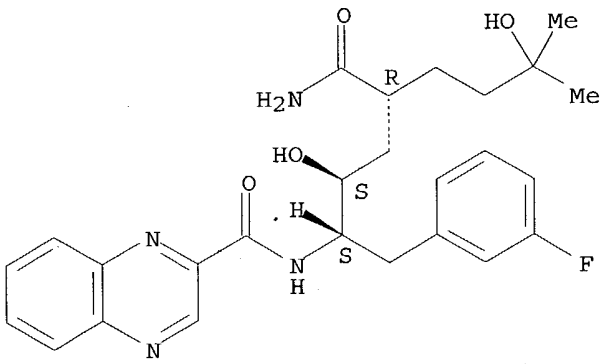
L50 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:913154 HCAPLUS
DOCUMENT NUMBER: 139:381369
TITLE: Process for preparation of 5-(1-amino-2-arylethyl)-3-(3-hydroxy-3-methylbutyl)dihydrofuran-2-ones via treatment of 5-(1-protected-amino-2-arylethyl)-3-(3-methyl-2-butenyl)dihydrofuran-2-ones with phosphoric acid
INVENTOR(S): Urban, Frank John; Jasys, Vytautas John; Li, Zhengong Bryan; Kath, John Charles
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003095440	A1	20031120	WO 2003-IB1840	20030505 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004019217	A1	20040129	US 2003-431276	20030507 <--

PRIORITY APPLN. INFO.: US 2002-380694P P 20020514 <--
US 2002-397138P P 20020718 <--

OTHER SOURCE(S): MARPAT 139:381369
IT **212790-31-3P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of aminoarylethylhydroxymethylbutyldihydrofuranones via treatment of protected aminoarylethylmethylbutenyldihydrofuranones with phosphoric acid)
RN 212790-31-3 HCAPLUS
CN 2-Quinoxalinecarboxamide, N-[(1S,2S,4R)-4-(aminocarbonyl)-1-[(3-fluorophenyl)methyl]-2,7-dihydroxy-7-methyloctyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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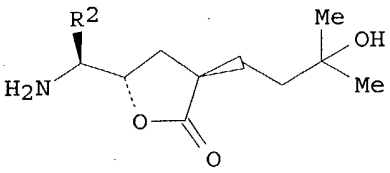

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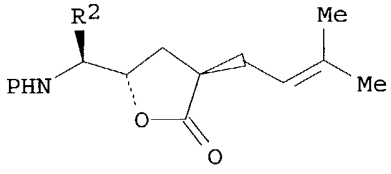


II

AB Title compds. [I; R2 = (substituted) Ph(CH2)m, naphthyl(CH2)m, cycloalkyl(CH2)m, alkyl(CH2)m, heteroaryl(CH2)m; m = 0-4] were prepared by treatment of alkenes (II; P = protecting group; R2 as above) with H3PO4. Thus, [2-(3-fluorophenyl)-1-[4-(3-methylbut-2-enyl)-5-oxotetrahydrofuran-2-yl]ethyl]carbamic acid tert-Bu ester (preparation given) was stirred with CH2Cl2 and 85% H3PO4 for 7h followed by cooling to 0°, dilution with water, and addition of 20% NaOH to pH 7-8.5 to give 5-[1-amino-2-(3-fluorophenyl)ethyl]-3-(3-hydroxy-3-methylbutyl)dihydrofuran-2-one. The latter was used to prepare quinoxaline-2-carboxylic acid [2-(3-fluorophenyl)-1-[4-(3-hydroxy-3-methylbutyl)-5-oxotetrahydrofuran-2-yl]ethyl]amide.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:434529 HCAPLUS
DOCUMENT NUMBER: 139:22107
TITLE: Preparation of benzamide derivatives as inhibitors of Asp-2
INVENTOR(S): Faller, Andrew; MacPherson, David Timothy; Milner, Peter Henry; Stanway, Steven James; Trouw, Leontine Saskia
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045913	A1	20030605	WO 2002-EP13515	20021129 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-28748 A 20011130 <--
GB 2002-14090 A 20020618 <--

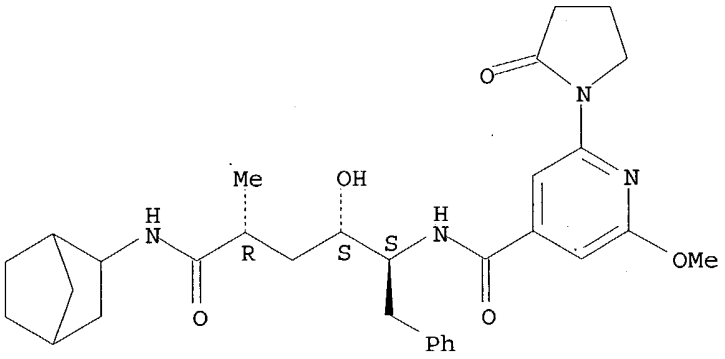
OTHER SOURCE(S): MARPAT 139:22107

IT **539821-13-1P**
RL: PAC (Pharmacological activity); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of benzamide derivs. as inhibitors of Asp-2)

RN 539821-13-1 HCAPLUS

CN 4-Pyridinecarboxamide, N-[(1S,2S,4R)-5-(bicyclo[2.2.1]hept-2-ylamino)-2-hydroxy-4-methyl-5-oxo-1-(phenylmethyl)pentyl]-2-methoxy-6-(2-oxo-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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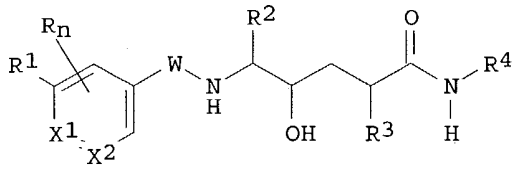

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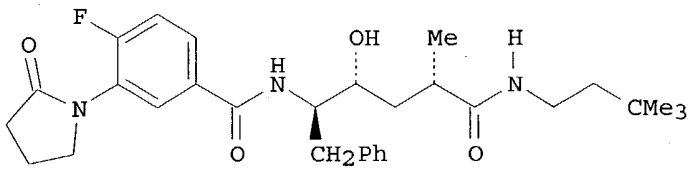


II

AB Benzamides I [X1, X2 = N, (un)substituted CH; W = CO, SO2; R = halogen; R1 = 2-oxo-substituted N heterocyclic; R2 = alkyl, aralkyl, heterocyclylalkyl, cycloalkylalkyl, arylthioalkyl, aryloxyalkyl, heterocyclylthioalkyl, heterocyclyloxyalkyl; R3 = (un)substituted alkyl, propargyl; R4 = (un)substituted alkyl; n = 0-2], having Asp-2 (β-secretase, BACE1 or Memapsin) inhibitory activity, useful in the treatment of diseases characterized by elevated β-amyloid levels or β-amyloid deposits, particularly Alzheimer's disease, were prepared Thus, tert.-Bu [(S)-1-(4-methyl-5-oxotetrahydrofuran-2-yl)-2-phenylethyl]carbamate was treated with Me3CCH2CH2NH2 and deblocked to give (2R,4S,5S)-H2NCH(CH2Ph)CH(OH)CH2CHMeCH2CH2CMe3 which was acylated with 3,4-Br(F)C6H3CO2H and treated with 2-pyrrolidinone to give the benzamide II. II had an IC50 for inhibition of Asp-2 of 600 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:434521 HCAPLUS
DOCUMENT NUMBER: 139:22015
TITLE: N-Carbamoylalkylcarboxamides and -sulfonamides with Asp-2 inhibitory activity
INVENTOR(S): Faller, Andrew; Milner, Peter Henry; Ward, John Gerard
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003045903	A1	20030605	WO 2002-EP13517	20021129 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT,

TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-28746 A 20011130 <--
GB 2001-28747 A 20011130 <--
GB 2002-14088 A 20020618 <--

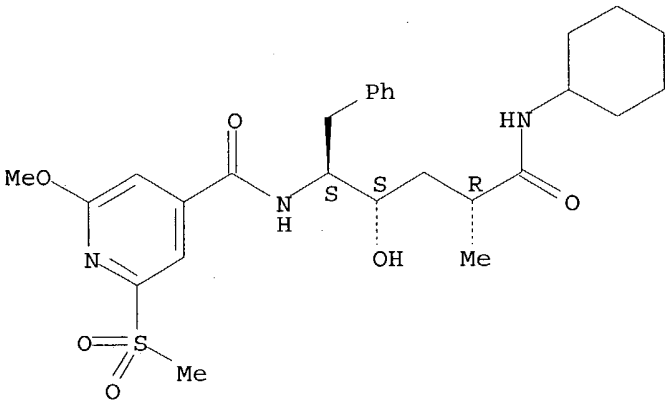
OTHER SOURCE(S): MARPAT 139:22015

IT **537031-91-7P**
RL: PAC (Pharmacological activity); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)** ; USES (Uses)
(preparation of N-carbamoylalkylcarboxamides and -sulfonamides with Asp-2 inhibitory activity)

RN 537031-91-7 HCAPLUS

CN 4-Pyridinecarboxamide, N-[(1S,2S,4R)-5-(cyclohexylamino)-2-hydroxy-4-methyl-5-oxo-1-(phenylmethyl)pentyl]-2-methoxy-6-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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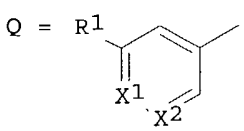
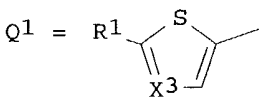




AB R1WNHCHR2CH(OH)CH2CHR3CONHR4 [R = Q, Q1; R1 = -SO2R5; X1-X3 = N, (un)substituted CH; W = CO, SO2; R2 = alkyl, aralkyl, heteocyclylalkyl, cycloalkylalkyl, arylthioalkyl, aryloxyalkyl, heteroarylthioalkyl, heteroaryloxyalkyl; R3 = alkyl, propargyl; R4 = alkyl, aralkyl, heteorcyclylalkyl, cycloakyl, cycloalkylalkyl, propargyl; R5 = Me, Et] having Asp-2 (β-secretase, BACE1 or Memapsin) inhibitory activity, useful in the treatment of diseases characterized by elevated

β-amyloid levels or β-amyloid deposits, particularly Alzheimer's disease, were prepared Thus, tert.-Bu [(S)-1-(4-methyl-5-oxotetrahydrofuran-2-yl)-2-phenylethyl]carbamate was treated with H2NCH2CH2CMe3 to give (2R,4S,5S)-PhCH2CH(NH2)CH(OH)CH2CHMeCONHCH2CH2CMe3 which was acylated with 3- MeSO2C6H4CO2H to give (1S,2S,4R)-3-MeSO2C6H4CONHCH(CH2Ph)CH(OH)CH2CHMeCONHCH2CH2CMe3 (I). I had an IC50 for Asp-2 inhibition of 400 nM.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:58078 HCAPLUS
DOCUMENT NUMBER: 138:137522
TITLE: Preparation of amine diols as β-secretase inhibitors for the treatment of Alzheimer's disease
INVENTOR(S): Schostarez, Heinrich Josef; Chrusciel, Robert Alan
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003006453	A1	20030123	WO 2002-US21709	20020710 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004019086	A1	20040129	US 2002-192543	20020710 <--
EP 1404664	A1	20040407	EP 2002-746943	20020710 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				

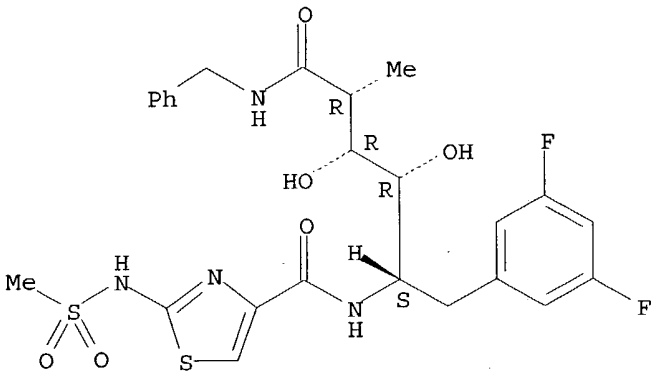
PRIORITY APPLN. INFO.: US 2001-304129P P 20010710 <--
WO 2002-US21709 W 20020710 <--

OTHER SOURCE(S): MARPAT 138:137522

IT **488805-23-8P**
RL: PAC (Pharmacological activity); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of diamine diols as β-secretase inhibitors to reduce Aβ-peptide production for treatment of Alzheimer's disease)

RN 488805-23-8 HCAPLUS
CN L-Idonamide, 2,5,6-trideoxy-6-(3,5-difluorophenyl)-2-methyl-5-[[[2-[(methylsulfonyl)amino]-4-thiazolyl]carbonyl]amino]-N-(phenylmethyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



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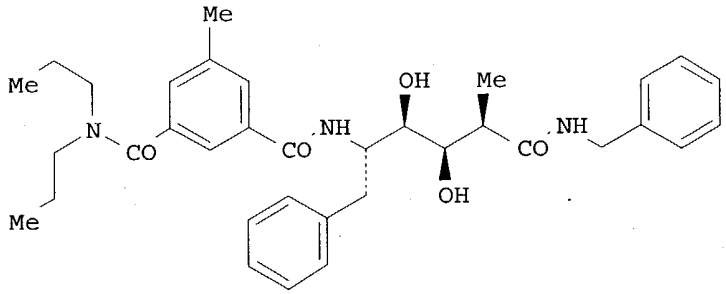

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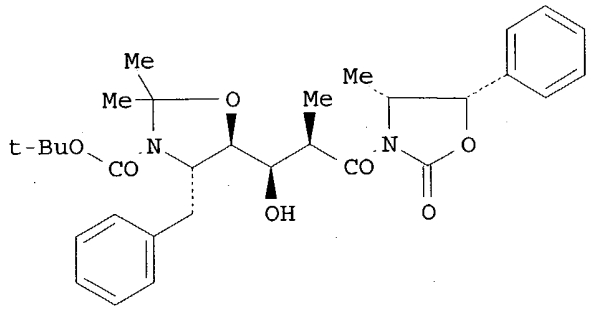


II

AB Diamine diols, such as R2RNNCH(R1)CH(OH)CH(OH)CH(R1')NR2RC [R1, R1' = alkyl, haloalkyl, alkoxyalkyl, alkylthioalkyl, arylalkyl, aryl, heteroaryl, heterocyclyl, etc.; R2 = H, alkyl; RC = H, arylaklyl, heteroarylalkyl, heterocyclylalkyl, etc.; RN = arylsulfonyl, heteroarylsulfonyl, acyl, etc.], were prepared as β-secretase inhibitors which inhibit the formation of Aβ-peptides for therapeutic use treating Alzheimer's disease, mild cognitive impairment Down's syndrome, hereditary cerebral hemorrhage with amyloidosis of the Dutch-Type, cerebral amyloid angiopathy, other degenerative dementias, dementias of mixed vascular and degenerative origin, dementia associated with Parkinson's disease, dementia associated with progressive supranuclear palsy, dementia associated with cortical basal degeneration, or diffuse Lewy body type of Alzheimer's disease. Thus, diamine diol I was prepared via reaction

of (4R,5S)-4-methyl-5-phenyl-3-propionyl-2-oxazolidinone with (4S,5R)-5-formyl-2,2-dimethyl-4-(phenylmethyl)-3-oxazolidinecarboxylic acid 1,1-dimethylethyl ester using Bu2BOTf and DIPEA in CH2Cl2 to form coupling product II. The 3-carbonyloxazolidin-2-one moiety of II was converted to the carboxylic acid using LiOH and hydrogen peroxide in MeOH, followed by amide formation of the carboxylic acid with PhCH2NH2 using DIEA and HATU in DMF, treatment redissolved amide with Dowex 50WX2-400 and MP-carbonate and, finally, N-acylation of the deprotected amine with 3-[(dipropylamino)carbonyl]-5-methylbenzoic acid using HCl in dioxane followed by treatment with HATU and DIEA and Dowex 50WX2-400 and MP-carbonate to give the desired I. The prepared diamine diols were assayed for their ability to inhibit β-secretase.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

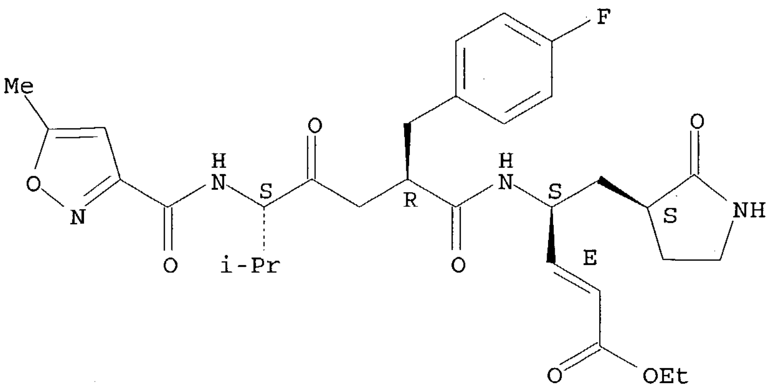
L50 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:717102 HCAPLUS
DOCUMENT NUMBER: 137:232922
TITLE: Efficient synthetic routes for the preparation of rhinovirus protease inhibitors and key intermediates
INVENTOR(S): Tian, Qingping; Nayyar, Naresh K.; Babu, Srinivasan; Tao, Junhua; Moran, Terence Jarold; Dagnino, Raymond; Mitchell, Lennert J.; Remarchuk, Travis Paul; Melnick, Michael Joseph; Bender, Steven Lee
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 25 pp., Cont.-in-part of U. S. 6,355,807.
CODEN: USXXCO
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
US 2002133020	A1	20020919	US 2001-984555	20011030	<--
US 6355807	B1	20020312	US 2000-643864	20000823	<--
US 2003064429	A1	20030403	US 2002-201944	20020725	<--

PRIORITY APPLN. INFO.:
US 1999-150358P P 19990824 <--
US 1999-150365P P 19990824 <--
US 2000-643864 A2 20000823 <--
US 2000-643865 B3 20000823 <--

OTHER SOURCE(S): CASREACT 137:232922
IT **223537-30-2P**, Ag7088
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of rhinovirus protease inhibitors and key intermediates)
RN 223537-30-2 HCAPLUS
CN 2-Pentenoic acid, 4-[[(2R,5S)-2-[(4-fluorophenyl)methyl]-6-methyl-5-[[(5-methyl-3-isoxazolyl)carbonyl]amino]-1,4-dioxoheptyl]amino]-5-[(3S)-2-oxo-3-pyrrolidinyl]-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB Syntheses of antipicornaviral agents R4CR5R6CONHCR2R3CR1:CZZ1 [R1 = H, F, alkyl, OH, SH, or an O-alkyl group; R2, R3 = CH2CH2CONH2 or CR2-A1X2, where R = H or alkyl and A1X2 is a ring in which A1 is CH or N and X2 is -CO-A4-A3n-A2- (n = 0-5; A2, A3 = CR2, NR, S, SO, SO2, or O; A4 = NH or NR); R4 is R9CONHCR7R8COCH2, where R7 and R8 are H, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, OH, alkoxy, SH, alkylthio, amino group, etc. and R9 is a five-membered heterocycle having 1-3 heteroatoms selected from O, N, and S; R5, R6 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; Z, Z1 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl group, heteroaryl, acyl, CN, etc. or Z1 and R1 or Z and Z1 form a cycloalkyl or heterocycloalkyl group] and key intermediates are described. Thus, a multistep synthesis of AG7088 is described in which the final step is coupling of (2E,4S)-4-amino-5-[(3S)-2-oxo-3-pyrrolidinyl]-2-pentenoic acid Et ester (preparation given) with (2R,5S)-2-[(4-fluorophenyl)methyl]-6-methyl-5-[[(5-methyl-3-isoxazolyl)carbonyl]amino]-4-oxoheptanoic acid.

L50 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:581874 HCAPLUS
DOCUMENT NUMBER: 135:152821
TITLE: Preparation of N-(hydroxyalkyl)quinoxaline-2-carboxamides and analogs as CCR1 antagonists for treatment of inflammation and other immune disorders
INVENTOR(S): Brown, Matthew Frank; Poss, Christopher Stanley
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

Applicants

PATENT NO.	KIND	DATE	).	DATE
WO 2001057023	A1	2001		20010126 <--

W: AE, AG, AL, AM, AT, ... BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, ... GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,

BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2001008002	A	20021029	BR 2001-8002	20010126	<--
EP 1252154	A1	20021030	EP 2001-901328	20010126	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003522164	T2	20030722	JP 2001-557855	20010126	<--
EE 200200432	A	20031215	EE 2002-432	20010126	<--
NZ 520075	A	20040227	NZ 2001-520075	20010126	<--
US 2002132810	A1	20020919	US 2001-774871	20010131	<--
US 6548671	B2	20030415			
BG 106922	A	20030331	BG 2002-106922	20020715	<--
ZA 2002006140	A	20030801	ZA 2002-6140	20020801	<--
NO 2002003675	A	20020910	NO 2002-3675	20020802	<--
US 2003204086	A1	20031030	US 2003-360059	20030206	<--
US 6689886	B2	20040210			

PRIORITY APPLN. INFO.:

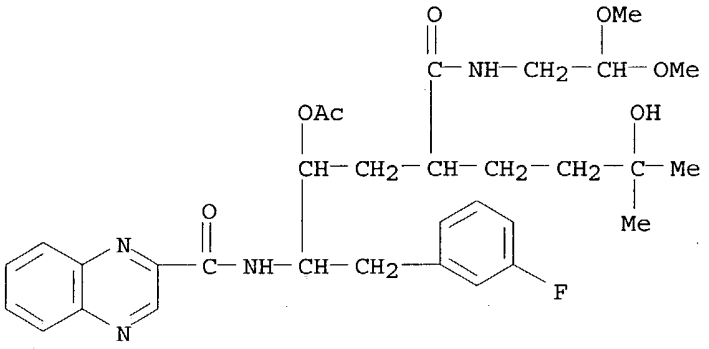
US 2000-180159P	P	20000204	<--
WO 2001-IB107	W	20010126	<--
US 2001-774871	A3	20010131	<--

OTHER SOURCE(S): MARPAT 135:152821

IT **352536-96-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(intermediate; preparation of N-(hydroxyalkyl)quinoxalinecarboxamide CCR1 antagonists from lactones for treatment of inflammation and other immune disorders)

RN 352536-96-0 HCAPLUS

CN 2-Quinoxalinecarboxamide, N-[2-(acetyloxy)-4-[[(2,2-dimethoxyethyl)amino]carbonyl]-1-[(3-fluorophenyl)methyl]-7-hydroxy-7-methyloctyl]- (9CI) (CA INDEX NAME)



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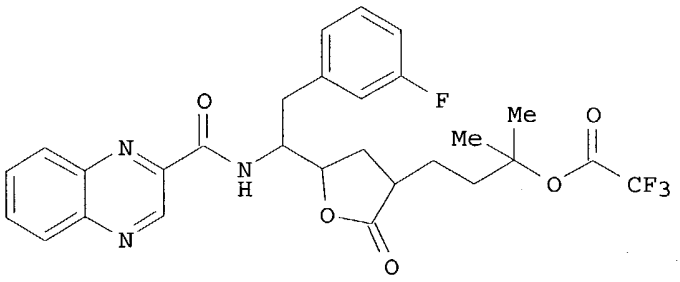

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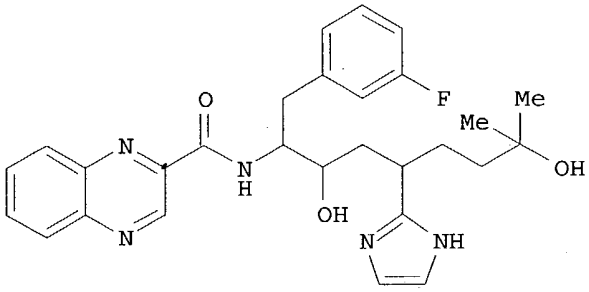


III

AB The title compds. R1CONHCHR2CH(OH)CH2CHR3R4 [I; wherein R1 = (un)substituted heteroaryl; R2 = (un)substituted Ph(CH2)m, naphthyl-(CH2)m, (cyclo)alkyl-(CH2)m, or heteroaryl-(CH2)m; m = 0-4; R3 = H, D, or (un)substituted alkyl, cycloalkyl-(CH2)n, heterocycloalkyl-(CH2)n, or (hetero)aryl-(CH2)n; n = 0-6; or R3 and the C to which it is attached form a 5-7 membered (un)substituted ring; R4 = heteroaryl, heterocycloalkyl, or (un)substituted sulfamoyl, thiocarbamoyl, or carboximidamide; stereoisomers or pharmaceutically acceptable salt thereof] were prepared as CCR1 antagonists for the treatment of inflammation and other immune disorders. For example, ring opening and amidation of the lactone II with aminoacetaldehyde di-Me acetal (91%), O-protection (96%), conversion to the imidazole using ammonium acetate in the presence of AcOH (17%), and deprotection (100%) gave III. All of the compds. of the invention that were tested for inhibition of chemotaxis of various chemokines exhibited IC50 < 25 μM.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:152861 HCAPLUS
DOCUMENT NUMBER: 134:208136
TITLE: Process for preparation of amidopentenoate peptide analog rhinovirus protease inhibitors.
INVENTOR(S): Tao, Junhua; Babu, Srinivasan; Dagnino, Raymond, Jr.; Tian, Qingping; Remarchuk, Travis Paul; McGee, Kevin Scott; Nayyar, Naresh K.; Moran, Terence Jarold
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014576	A2	20010301	WO 2000-US23032	20000823 <--
WO 2001014576	A3	20010830		
WO 2001014576	C1	20020620		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

BR 2000013323	A	20020402	BR 2000-13323	20000823 <--
EP 1206470	A2	20020522	EP 2000-955830	20000823 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

JP 2003511350	T2	20030325	JP 2001-518887	20000823 <--
ZA 2002000506	A	20030422	ZA 2002-506	20020121 <--
US 2003064429	A1	20030403	US 2002-201944	20020725 <--

PRIORITY APPLN. INFO.:	US 1999-150365P	P	19990824 <--
	US 1999-150358P	P	19990824 <--
	US 2000-643865	B3	20000823 <--
	WO 2000-US23032	W	20000823 <--

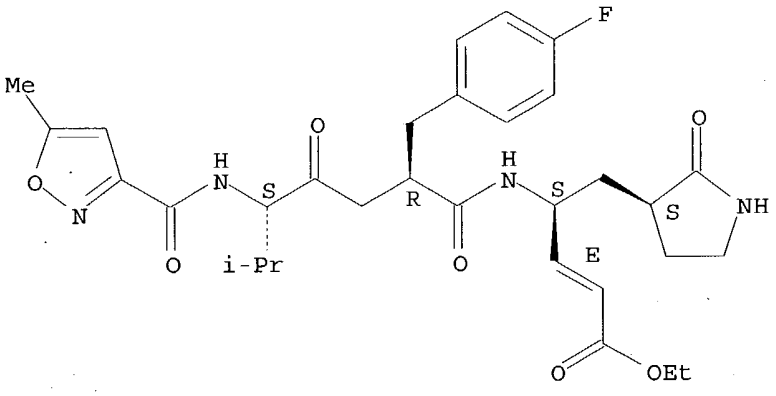
OTHER SOURCE(S): CASREACT 134:208136; MARPAT 134:208136

IT **223537-30-2P**, AG7088
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**
(process for preparation of amidopentenoate peptide analog rhinovirus protease inhibitors)

RN 223537-30-2 HCAPLUS

CN 2-Pentenoic acid, 4-[[(2R,5S)-2-[(4-fluorophenyl)methyl]-6-methyl-5-[[(5-methyl-3-isoxazolyl)carbonyl]amino]-1,4-dioxoheptyl]amino]-5-[(3S)-2-oxo-3-pyrrolidinyl]-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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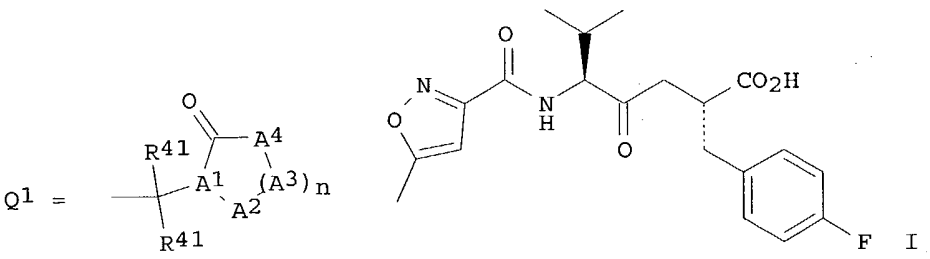


II

AB R4R6CHCONHCR2R3CR1:CZZ1 [R1 = H, F, alkyl, OH, SH, alkoxy; R2, R3 = H, H2NCOCH2CH2, Q1; R4 = R9CONHCR7R8COCH2; R6 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl; R7, R8 = H, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, OR17, SR17, NR17R18, NR19NR17R18, NR17OR18; R9 = 5-membered heterocyclyl; R17, R18, R19 = H, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, acyl; n = 0-5; A1 = CH, N; A2, A3 = C(R41)2, NR41, S, SO, SO2, O; A4 = NH, NR41; R41 = H, alkyl; Z, Z1 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, cyano, NO2, etc.; ZR1 or Z1R1 = atoms to form a cycloalkyl, heterocyclyl ring; R41 = H, alkyl], were prepared by preparation and coupling of R20NHCR7R8COCH2CHR6CO2H (R20 = R9CO; other variables as above) with H2NCR2R3CR1:CZZ1 (variables as above). Thus, intermediates (I) and (II) were stirred with N-methylmorpholine and CMDT in DMF at 0° to room temperature to give >85% title coupling product (AG7088) of >97% purity.

L50 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:152641 HCAPLUS
DOCUMENT NUMBER: 134:193743
TITLE: Synthetic routes for the preparation of rhinovirus protease inhibitors and key intermediates
INVENTOR(S): Tian, Qingping; Nayyar, Naresh K.; Babu, Srinivasan; Tao, Junhua; Moran, Terence Jarold; Dagnino, Raymond, Jr.; Mitchell, Lennert J.; Remarchuk, Travis Paul; Melnick, Michael Joseph; Bender, Steven Lee
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001014329	A1	20010301	WO 2000-US23033	20000823	<--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1206450	A1	20020522	EP 2000-955831	20000823	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL					
BR 2000013306	A	20020528	BR 2000-13306	20000823	<--
JP 2003507453	T2	20030225	JP 2001-518419	20000823	<--
AU 770221	B2	20040219	AU 2000-67971	20000823	<--
ZA 2002000504	A	20030121	ZA 2002-504	20020121	<--
US 2003064429	A1	20030403	US 2002-201944	20020725	<--
PRIORITY APPLN. INFO.:			US 1999-150358P	P 19990824	<--
			US 1999-150365P	P 19990824	<--
			US 2000-643865	B3 20000823	<--
			WO 2000-US23033	W 20000823	<--

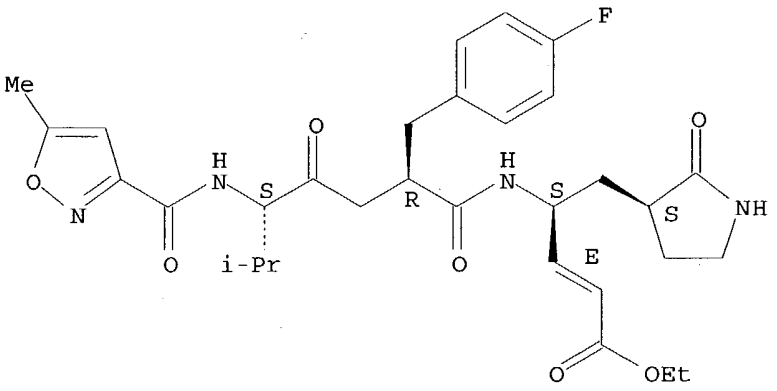
OTHER SOURCE(S): CASREACT 134:193743; MARPAT 134:193743

IT **223537-30-2P**, Ag7088
RL: **IMF (Industrial manufacture)**; **SPN (Synthetic preparation)**; **PREP (Preparation)**; BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of rhinovirus protease inhibitors and key intermediates)

RN 223537-30-2 HCAPLUS

CN 2-Pentenoic acid, 4-[[(2R,5S)-2-[(4-fluorophenyl)methyl]-6-methyl-5-[[(5-methyl-3-isoxazolyl)carbonyl]amino]-1,4-dioxoheptyl]amino]-5-[(3S)-2-oxo-3-pyrrolidinyl]-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



AB Syntheses of antipicornaviral agents R4CR5R6CONHCR2R3CR1:CZZ1 [R1 = H, F, alkyl, OH, SH, or an O-alkyl group; R2, R3 = CH2CH2CONH2 or CR2-A1X2, where R = H or alkyl and A1X2 is a ring in which A1 is CH or N and X2 is -CO-A4-A3n-A2- (n = 0-5; A2, A3 = CR2, NR, S, SO, SO2, or O; A4 = NH or NR); R4 is R9CONHCR7R8COCH2, where R7 and R8 are H, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, OH, alkoxy, SH, alkylthio, amino group, etc. and R9 is a five-membered heterocycle having 1-3 heteroatoms

selected from O, N, and S; R5, R6 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, or heteroaryl; Z, Z1 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl group, heteroaryl, acyl, CN, etc. or Z1 and R1 or Z and Z1 form a cycloalkyl or heterocycloalkyl group] and key intermediates are described. Thus, a multistep synthesis of AG7088 is described in which the final step is coupling of (2E,4S)-4-amino-5-[(3S)-2-oxo-3-pyrrolidinyl]-2-pentenoic acid Et ester (preparation given) with (2R,5S)-2-[(4-fluorophenyl)methyl]-6-methyl-5-[[(5-methyl-3-isoxazolyl)carbonyl]amino]-4-oxoheptanoic acid.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:723052 HCAPLUS
DOCUMENT NUMBER: 131:337357
TITLE: Preparation of peptides as antipicornaviral agents
INVENTOR(S): Dragovich, Peter Scott; Marakovits, Joseph Timothy; Prins, Thomas Jay; Tikhe, Jayashree Girish; Webber, Stephen Evan; Zhou, Ru; Johnson, Theodore O.
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9957135	A1	19991111	WO 1999-US260	19990105 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2326763	AA	19991111	CA 1999-2326763	19990105 <--
AU 9920287	A1	19991123	AU 1999-20287	19990105 <--
AU 768539	B2	20031218		
BR 9910573	A	20010116	BR 1999-10573	19990105 <--
EP 1073672	A1	20010207	EP 1999-900780	19990105 <--
EP 1073672	B1	20030827		
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SI 20428	C	20010630	SI 1999-20041	19990105 <--
TR 200003159	T2	20010921	TR 2000-20000315919990105 <--	
LT 4846	B	20011025	LT 2000-20000010919990105 <--	
EE 200000621	A	20020617	EE 2000-621	19990105 <--
EP 1329457	A2	20030723	EP 2003-9409	19990105 <--
EP 1329457	A3	20030730		
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JP 2003526600	T2	20030909	JP 2000-547104	19990105 <--
AT 248186	E	20030915	AT 1999-900780	19990105 <--
NZ 507633	A	20031031	NZ 1999-507633	19990105 <--
PT 1073672	T	20040130	PT 1999-900780	19990105 <--
ZA 9903000	A	20000120	ZA 1999-3000	19990429 <--
US 6531452	B1	20030311	US 1999-301977	19990429 <--

HR 2000000623	A1	20010430	HR 2000-623	20000920	<--
NO 2000005411	A	20001027	NO 2000-5411	20001027	<--
BG 104899	A	20010831	BG 2000-104899	20001101	<--
LV 12666	B	20011120	LV 2000-162	20001219	<--
HK 1034722	A1	20031128	HK 2001-105452	20010806	<--
US 2003130204	A1	20030710	US 2002-289982	20021106	<--

PRIORITY APPLN. INFO.:

US 1998-83828P	P	19980430	<--
US 1998-98358P	P	19980828	<--
EP 1999-900780	A3	19990105	<--
WO 1999-US260	W	19990105	<--
US 1999-301977	A3	19990429	<--

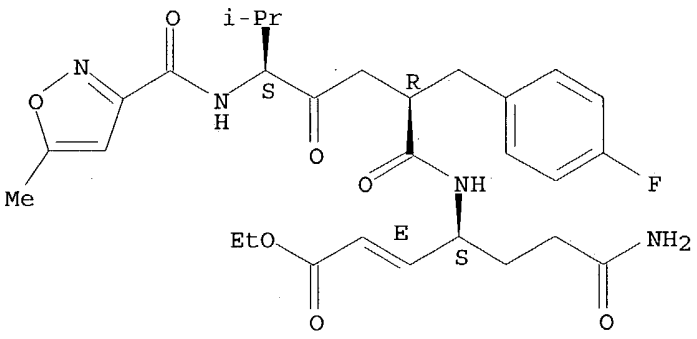
OTHER SOURCE(S): MARPAT 131:337357

IT **214286-28-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; **SPN (Synthetic preparation)**; THU (Therapeutic use); **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent); USES (Uses)
(preparation of peptides as antipicornaviral agents and protease inhibitors)

RN 214286-28-9 HCAPLUS

CN 2-Heptenoic acid, 7-amino-4-[[(2R,5S)-2-[(4-fluorophenyl)methyl]-6-methyl-5-[[(5-methyl-3-isoxazolyl)carbonyl]amino]-1,4-dioxoheptyl]amino]-7-oxo-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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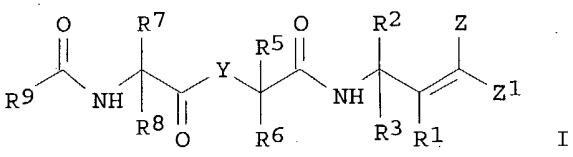


I

AB Peptido and peptido-mimetic compds. I (Y = O, substituted N or C; R1 = H, F, alkyl, OH, SH, alkoxy; R2, R3 = independently H, CH2Ch2CONH2, heterocycle; R5, R6 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl; R7, R8 = independently H, alkyl, cycloalkyl, heterocycloalkyl, aryl,, heteroaryl, OH, alkoxy, alkylthio, alkylamine, alkoxyamine; R9 = 5-membered heterocycle; Z, Z1 = independently H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, acyl, ester, amide, sulfone) were prepared and advantageously inhibit or block the biol. activity of the

picornaviral 3C protease. These compds., as well as pharmaceutical compns. containing these compds., are useful for treating patients or hosts infected with one or more picorna-viruses, such as RVP. Thus, ethyl-3-{Cbz-L-Leu-L-Phe-L-((R)-Pyrrol-Ala)}-E-propenoate was prepared as antipicornaviral agent and protease inhibitor (Kobs/I = 18000 M-1 x sec-1).

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:511130 HCAPLUS
DOCUMENT NUMBER: 131:157767
TITLE: Preparation of quinoxalinecarboxylic acid 4-carbamoyl-2,7-dihydroxy-7-methyloctylamides for treatment of inflammation and immune disorders.
INVENTOR(S): Kath, John Charles; Brown, Matthew Frank; Poss, Christopher Stanley
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9940061	A2	19990812	WO 1999-IB67	19990118 <--
WO 9940061	A3	19991021		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2320388	AA	19990812	CA 1999-2320388	19990118 <--
AU 9917789	A1	19990823	AU 1999-17789	19990118 <--
AU 752407	B2	20020919		
BR 9907655	A	20001024	BR 1999-7655	19990118 <--
EP 1051405	A2	20001115	EP 1999-900098	19990118 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
TR 200002248	T2	20001221	TR 2000-200002248	19990118 <--
JP 2002502839	T2	20020129	JP 2000-530493	19990118 <--
NZ 505724	A	20030228	NZ 1999-505724	19990118 <--
TW 470744	B	20020101	TW 1999-88101505	19990201 <--
ZA 9900873	A	20000804	ZA 1999-873	19990204 <--
AP 992	A	20010806	AP 1999-1457	19990204 <--
W: BW, GM, GH, KE, MW, SD, UG, ZM, ZW				
US 6673801	B1	20040106	US 2000-403218	20000302 <--
NO 2000003965	A	20001003	NO 2000-3965	20000804 <--
HR 2000000529	A1	20010831	HR 2000-529	20000804 <--
BG 104726	A	20010430	BG 2000-104726	20000829 <--
US 2003018033	A1	20030123	US 2002-200844	20020722 <--

PRIORITY APPLN. INFO.:
US 1998-73801P P 19980205 <--
WO 1999-IB67 W 19990118 <--
US 2000-403218 A1 20000302 <--

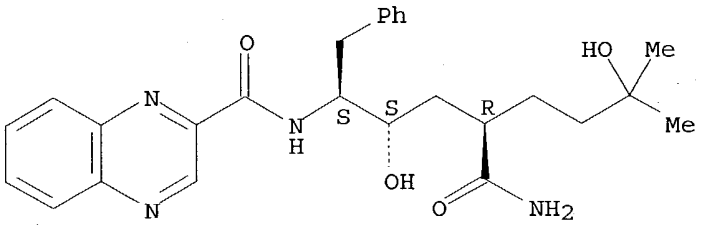
IT **212790-30-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of quinoxalinecarboxylic acid 4-carbamoyl-2,7-dihydroxy-7-methyloctylamides for treatment of inflammation and immune disorders)

RN 212790-30-2 HCAPLUS

CN 2-Quinoxalinecarboxamide, N-[(1S,2S,4R)-4-(aminocarbonyl)-2,7-dihydroxy-7-methyl-1-(phenylmethyl)octyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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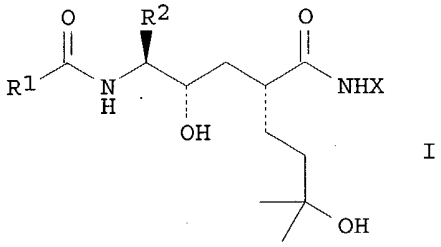


I

AB Title compds. (I; all variables undefined), were prepared as antagonists of CCR1 receptors. Thus, [1(S)-[5-oxotetrahydrofuran-2(S)-yl]-2-phenylethyl]carbamic acid tert-Bu ester in THF was added dropwise to a mixture of BuLi and HN(SiMe3)2 in THF at -78°; 4-bromo-2-methyl-2-butane in THF was added after 30 min. and the mixture was stirred 3h to -60° to give 77% [1(S)-[4(R)-(3-methylbut-2-enyl)-5-oxotetrahydrofuran-2(S)-yl]-2-phenylethyl]carbamic acid tert-Bu ester. The latter was stirred with CF3CO2H and the residue was stirred with 2-quinoxalyl chloride and Et3N in CH2Cl2 to give 72% quinoxaline-2-carboxylic acid 1(S)-benzyl-4(R)-carbamoyl-2(S),7-dihydroxy-7-methyloctylamide. Tested I inhibited chemotaxis with IC50 <25 μM.

L50 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:64823 HCAPLUS

DOCUMENT NUMBER: 130:125408

TITLE: Preparation of polyol-amino acid compounds having activity against Helicobacter pylori

INVENTOR(S): Miyagawa, Ken-ichiro; Tsubotani, Shigetoshi; Nakao, Masafumi; Nakano, Yoshitaka; Kamiyama, Keiji; Izawa, Motoo; Akiyama, Yohko; Nishikimi, Yuji

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: PCT Int. Appl., 178 pp.
CODEN: PIXXD2

DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9902549	A1	19990121	WO 1998-JP3066	19980708	<--
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
AU 9881273	A1	19990208	AU 1998-81273	19980708	<--
JP 11080109	A2	19990326	JP 1998-193489	19980708	<--
EP 998488	A1	20000510	EP 1998-931013	19980708	<--
EP 998488	B1	20040317			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
AT 261986	E	20040415	AT 1998-931013	19980708	<--
ZA 9806079	A	20000110	ZA 1998-6079	19980709	<--
TW 479054	B	20020311	TW 1998-87111146	19980709	<--
US 6423869	B1	20020723	US 1999-423118	19991101	<--

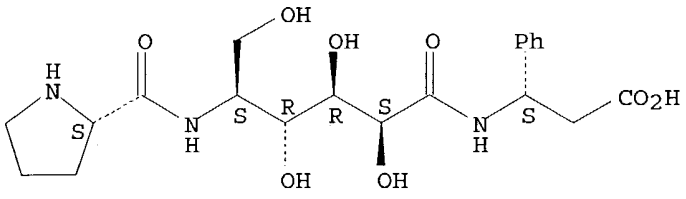
PRIORITY APPLN. INFO.: JP 1997-184086 A 19970709 <--
WO 1998-JP3066 W 19980708 <--

OTHER SOURCE(S): MARPAT 130:125408

IT **219813-10-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(fermentative preparation and chemical modification of polyol-amino acid compds. having activity against Helicobacter pylori)

RN 219813-10-2 HCAPLUS
CN β-Alanine, L-prolyl-5-amino-5-deoxy-L-galactonoyl-3-phenyl-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



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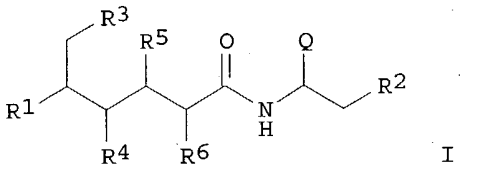

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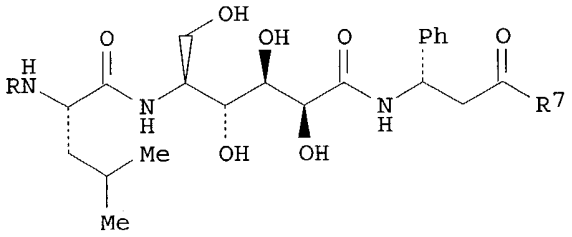


II

AB Title compds. I [R1 = (un)substituted amino, (un)substituted amino acid residue, (un)substituted peptide residue; R2 = optionally esterified or amidated carboxy; R3, R4, R5, R6 independently = (un)protected OH; Q = (un)substituted aryl] or a salt thereof, isolated from Bacillus cultures and chemical modified, are described. I possess anti-Helicobacter pylori activity, and useful in the prevention or treatment of various diseases associated with Helicobacter bacteria, such as duodenal ulcer, gastric ulcer, chronic gastritis, and cancer of the stomach. Thus, leucine-polyol conjugate II (R = H, R7 = OH) (HC-70III), isolated from Bacillus sp. HC-70 or from Bacillus insolitus HC-72, underwent N-terminal peptide coupling with a variety of amino acid derivs., or amidation or esterification at the C-terminus to give a variety of derivs., e.g. II [R = H, PhCH2O2C (Cbz), H-Ala, H-Sar, H-Phe, H-Lys, H-Glu, H-Orn, H-Asn, H-Gln, H-Thr, H-Leu, H-Ile, H-Ser(Me), H-Val, H-Nva, H-Nle, H-D-Ala, R7 = OH, OCHPh2, OEt, OCH2OCMe3, NH2]. A variety of pharmaceutical formulations containing I (R = H, R7 = OH) are given.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:682224 HCAPLUS
DOCUMENT NUMBER: 129:290442
TITLE: Preparation of alkene-ketomethylene pseudopeptides as picornavirus 3C protease inhibitors
INVENTOR(S): Dragovich, Peter S.; Prins, Thomas J.; Zhou, Ru
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843950	A1	19981008	WO 1998-US6018	19980326 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,

KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI,
FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM,
GA, GN, ML, MR, NE, SN, TD, TG

US 6020371	A	20000201	US 1997-991282	19971216	<--
AU 9867788	A1	19981022	AU 1998-67788	19980326	<--
AU 736550	B2	20010802			
EP 975588	A1	20000202	EP 1998-913173	19980326	<--
EP 975588	B1	20030903			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AT 248809	E	20030915	AT 1998-913173	19980326	<--
US 6331554	B1	20011218	US 1999-421560	19991020	<--
US 2002032237	A1	20020314	US 2001-947381	20010907	<--
US 6649639	B2	20031118			
US 2004072907	A1	20040415	US 2003-629657	20030730	<--

PRIORITY APPLN. INFO.:	US 1997-825331	A2	19970328 <--
	US 1997-46204P	P	19970512 <--
	US 1997-991282	A	19971216 <--
	WO 1998-US6018	W	19980326 <--
	US 1999-421560	A3	19991020 <--
	US 2001-947381	A3	20010907 <--

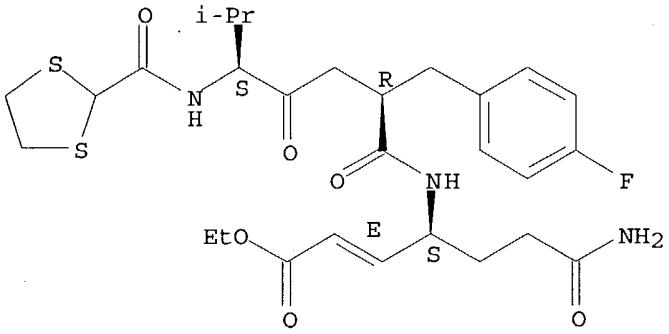
OTHER SOURCE(S): MARPAT 129:290442

IT **214286-21-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of alkene-ketomethylene pseudopeptides as picornavirus 3C protease inhibitors)

RN 214286-21-2 HCAPLUS

CN 2-Heptenoic acid, 7-amino-4-[[(2R,5S)-5-[(1,3-dithiolan-2-ylcarbonyl)amino]-2-[(4-fluorophenyl)methyl]-6-methyl-1,4-dioxoheptyl]amino]-7-oxo-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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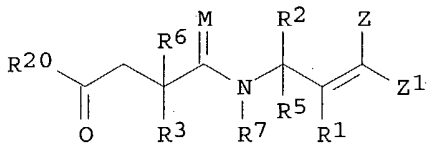

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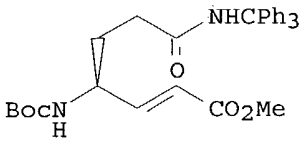

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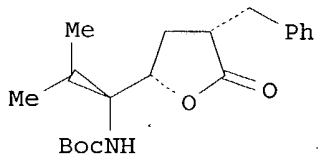
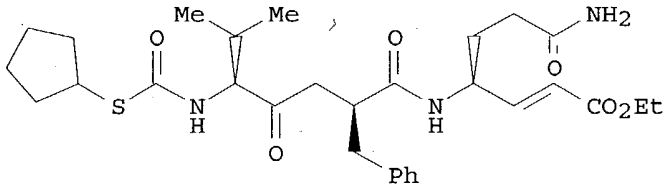


III



IV

AB Picornaviral 3C protease inhibitors I [M = O, S; R1 = H, F, alkyl, OH, SH, O-alkyl; R2, R5 = H, XY1A1(B1)D1, alkyl different from XY1A1(B1)D1, with the proviso that both R2 and R5 ≠ H and when R2 or R5 = XY1A1(B1)D1, X = CH or CF and Y1 = CH or CF; R3, R6 = H, F, alkyl; R20 = H, OH, suitable organic moiety; Z, Z1 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, etc; XY1 form 3-membered ring with Q1, Q1 = CR10R11, O, X = CH, CF, Y = CH, CF, C-alkyl; R10, R11 = H, halo, alkyl; CR10R11 = cycloalkyl, heterocycloalkyl; X = CH2, CF2, CHF, S; Y1 = O, S, NR12, CR12R14, CO, CS, C(CR13R14); R12 = H, alkyl; R13, R14 = H, F, alkyl; CR13R14 = cycloalkyl, heterocycloalkyl; A1 = C, CH, CF, S, P, Se, N, NR15, S(O), Se(O), P(OR15), P(NR15R16); R15, R16 = alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl; D1 = moiety containing electron lone pair capable of forming H bond; B1 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, OR17, SR17, NR1718, NR19NR17R18, NR17OR18; R17-R19 = H, any group R15; with provisos], and pharmaceutically acceptable salts thereof and prodrugs thereof, obtainable by chemical synthesis, inhibit or block the biol. activity of picornaviral 3C proteases. These compds., as well as pharmaceutical compns. that contain these compds., are suitable for treating patients or hosts infected with one or more picornaviruses. Several novel methods and intermediates can be used to prepare the novel picornaviral 3C protease inhibitors of the present invention. Thus, olefination of protected glutamine aldehyde Boc-Gln(CPh3)-H (Boc = Me3CO2C), prepared in 3 steps from Boc-Gln(CPh3)-OH, with tri-Et phosphonoacetate gave (E)-alkene dipeptide isostere II. Deprotection of II and coupling with lactone III [prepared in 6 steps from isobutyraldehyde, vinylmagnesium bromide, di-Et malonate, (1R,2R)-pseudoephedrine, and benzyl bromide], followed by oxidation, deprotection, thiocarbamoylation with cyclopentyl thiolformate, and detritylation gave desired pseudopeptide IV. IV and 33 related alkene-ketomethylene pseudopeptides were tested for inhibition of rhinovirus protease, antirhinoviral activity, and anticoxsackieviral activity, with IV showing EC50 = 0.022 μM and 0.16 μM for antirhinoviral and anticoxsackieviral activity, resp.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

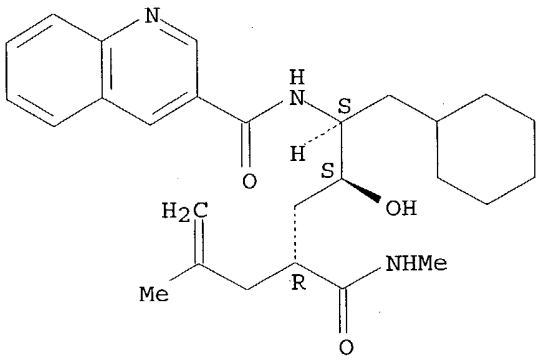
L50 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:608600 HCAPLUS
DOCUMENT NUMBER: 129:230740
TITLE: Heteroaryl-hexanoic acid amide derivatives, their preparation and their use as selective inhibitors of MIP-1α binding to its CCR1 receptor
INVENTOR(S): Brown, Matthew Frank; Kath, John Charles; Poss, Christopher Stanley
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9838167	A1	19980903	WO 1998-US1568	19980205	<--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9861354	A1	19980918	AU 1998-61354	19980205	<--
AU 745687	B2	20020328			
EP 966443	A1	19991229	EP 1998-906013	19980205	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO					
TR 9902056	T2	20000121	TR 1999-9902056	19980205	<--
BR 9807858	A	20000222	BR 1998-7858	19980205	<--
JP 2000513740	T2	20001017	JP 1998-537644	19980205	<--
ZA 9801602	A	19990921	ZA 1998-1602	19980226	<--
AP 1056	A	20020405	AP 1998-1200	19980226	<--
W: BW, GM, KE, MW, UG, ZM, ZW					
BG 103688	A	20001130	BG 1999-103688	19990824	<--
NO 9904101	A	19990825	NO 1999-4101	19990825	<--
US 6403587	B1	20020611	US 2000-380269	20000518	<--
US 2002198207	A1	20021226	US 2002-154145	20020522	<--

PRIORITY APPLN. INFO.:
US 1997-39169P P 19970226 <--
WO 1998-US1568 W 19980205 <--
US 2000-380269 A3 20000518 <--

OTHER SOURCE(S): MARPAT 129:230740
IT **212787-52-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of heteroaryl-substituted hexanamides and their use as selective inhibitors of MIP-1α binding to its CCR1 receptor)
RN 212787-52-5 HCAPLUS
CN 3-Quinolinecarboxamide, N-[(1S,2S,4R)-1-(cyclohexylmethyl)-2-hydroxy-6-methyl-4-[(methylamino)carbonyl]-6-heptenyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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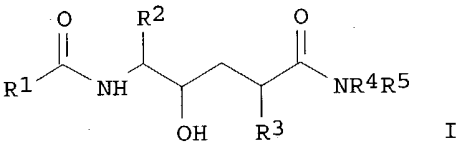


I

AB I [R1 = optionally substituted (C2-C9)heteroaryl; R2 = optionally substituted phenyl-(CH2)m-, naphthyl-(CH2)m-, (C3-C10)cycloalkyl-(CH2)m-, (C1-C6)alkyl or (C2-C9)heteroaryl-(CH2)m-; m = integer from zero to four; R3 = H, optionally substituted (C1-C10)alkyl, (C3-C10)cycloalkyl-(CH2)n-, (C2-C9)heterocycloalkyl-(CH2)n-, (C2-C9)heteroaryl-(CH2)n-, aryl-(CH2)n-; n = integer from zero to six; R3 and the carbon to which it is attached form an optionally substituted and/or fused five to seven membered carbocyclic ring; R4 = H, (C1-C6)alkyl, hydroxy, (C1-C6)alkoxy, hydroxy-(C1-C6)alkyl, (C1-C6)alkoxyCO, (C3-C10)cycloalkyl-(CH2)p-, optionally substituted (C2-C9)heterocycloalkyl-(CH2)p-, (C2-C9)heteroaryl-(CH2)p-, phenyl-(CH2)p- or naphthyl-(CH2)p-, p = integer from zero to four; R4 and R5 together with the nitrogen atom to which they are attached form an optionally substituted (C2-C9)heterocycloalkyl group; R5 = H, (C1-C6)alkyl, amino] were prepared The present compds. are potent and selective inhibitors of MIP-1α binding to its receptor CCR1, and are thus useful to treat inflammation and other immune disorders. E.g., quinoxaline-2-carboxylic acid [1(S)-benzyl-4(R)-benzylcarbamoyl-7-fluoro-2(S)-hydroxy-7-methyloctyl]amide was prepared

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:207292 HCAPLUS
DOCUMENT NUMBER: 128:270871
TITLE: Preparation of azolyl dipeptide analogs as retroviral protease inhibitors
INVENTOR(S): Carr, Thomas Joseph; Demarsh, Peter Lawrence; Dreyer, Geoffrey Bainbridge; Fenwick, Ashley Edward
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: U.S., 42 pp., Cont. of U.S. Ser. No. 193.026, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

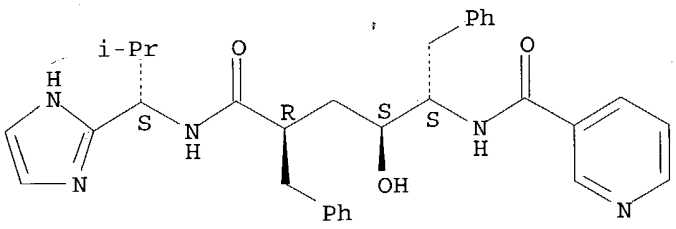
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5733882	A	19980331	US 1995-396356	19950228 <--
			US 1994-193026	19940117 <--

PRIORITY APPLN. INFO.:
OTHER SOURCE(S): MARPAT 128:270871

IT **149356-87-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of azolyl dipeptide analogs as retroviral protease inhibitors)

RN 149356-87-6 HCAPLUS
CN 3-Pyridinecarboxamide, N-[2-hydroxy-5-[[1-(1H-imidazol-2-yl)-2-methylpropyl]amino]-5-oxo-1,4-bis(phenylmethyl)pentyl]-, [1S-[1R*,2R*,4S*,5(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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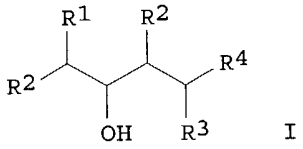

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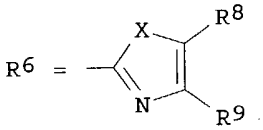

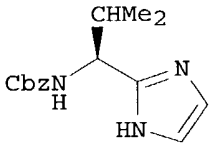

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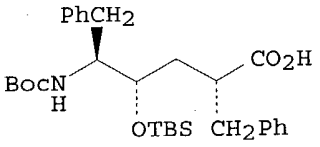
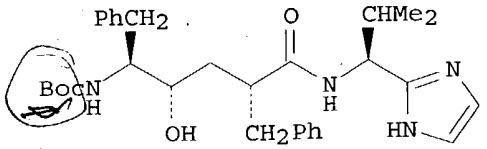


III



IV

AB The present invention provides compds., more particularly dipeptide analogs I [R1, R3 = independently (un)substituted Q, Q-C1-6 alkyl, Q-C2-6 alkenyl, Q-C2-6 alkynyl, C1-6 alkyl substituted by 1-5 F atoms; Q = H, C3-6 cycloalkyl, C5-6 cycloalkenyl, aryl, heterocyclyl; R2 = H, OH; R4 = R6NR11, CONR11CHR6R7; R5 = R6NR11, R10NR11; X = NR11, O, S; R7 = Q, Q-C1-6 alkyl, Q-C2-6 alkenyl; R8, R9 = independently H, OH, halo, NO2, acyl, CF3, aryl, etc.; R8R9 = fused C2-4 alkylene, aryl, heterocyclyl; R10 = A-(B)n; R11 = H, C1-4 alkyl; B = amino acid; A = H, (un)substituted aryl, heterocyclyl, aryl-W, heterocyclyl-W, phthaloyl, etc.; W = CO, O2C, NR11CO, SCO, NR11CS, SO2, NR11SO2, P(O)(OR22); R22 = H, C1-6 alkyl, Ph, phenyl-C1-4 alkyl; with provisos], or a pharmaceutically acceptable salt thereof, which bind to retroviral proteases. These compds. are inhibitors of retroviral proteases and are useful for treating diseases related to infection by retroviruses. Thus, cyclocondensation of protected valinal Z-Val-H (Z = PhCH2O2C) with ammonia and glyoxal gave imidazole II. Deprotection of II, followed by coupling with dipeptide isostere III, and final desilylation gave desired title compound IV as its HCl salt. The prepared compds., including IV, showed inhibition of HIV-1 protease with Ki = 1 nM to 5 μM, and inhibited infection of cells with the HIV virus with IC50 = 0.1 to 10 μM.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L50 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:547277 HCAPLUS
DOCUMENT NUMBER: 127:162122
TITLE: Preparation of 5-amino-4-hydroxyhexanoic acid derivatives for treatment of AIDS
INVENTOR(S): Bold, Guido; Lang, Marc; Fassler, Alexander; Capraro, Hans-georg; Bhagwat, Shripad; Schneider, Peter; Hoogevest, Petervan
PATENT ASSIGNEE(S): Ciba-Geigy Corp., USA
SOURCE: U.S., 98 pp., Cont.-in-part of U.S. Ser. No. 941,595, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

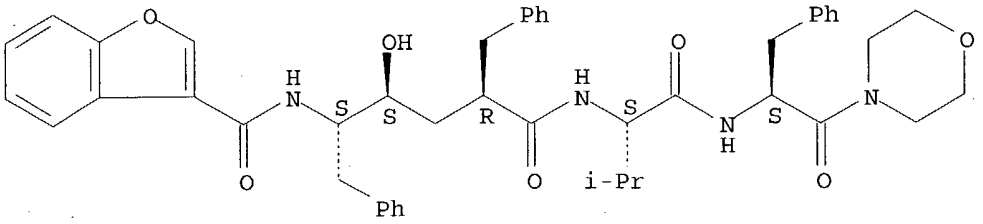
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5643878	A	19970701	US 1994-207646	19940308 <--
ZA 9206938	A	19940311	ZA 1992-6938	19920911 <--
CN 1089269	A	19940713	CN 1993-100044	19930104 <--

PRIORITY APPLN. INFO.:
CH 1991-2689 A 19910912 <--
CH 1992-890 A 19920327 <--
CH 1992-2007 A 19920625 <--
US 1992-941595 B2 19920908 <--
CH 1992-772 A 19930311 <--

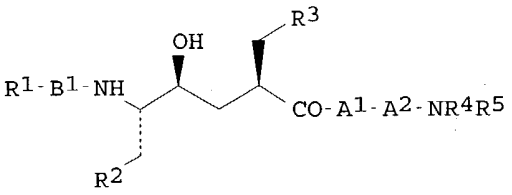
OTHER SOURCE(S): MARPAT 127:162122
IT **150608-90-5P**
RL: **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of aminohydroxyhexanoic acid derivs. for treatment of AIDS)
RN 150608-90-5 HCAPLUS
CN 3-Benzofurancarboxamide, N-[2-hydroxy-5-[[2-methyl-1-[[[2-(4-morpholinyl)-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]propyl]amino]-5-oxo-1,4-

bis(phenylmethyl)pentyl]-, [1S-[1R*,2R*,4S*,5[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI



I

AB Peptides I [A1, B1 = bond, amino acid residue; A2 = amino acid residue; R1 = H, alkoxycarbonyl, or (un)substituted benzyloxycarbonyl; R2, R3 = (un)substituted Ph or cyclohexyl; R4R5N = (un)substituted morpholino] were prepared for the treatment of AIDS. Thus, 5(S)-Boc-amino-4(S)-hydroxy-6-cyclohexyl-2(R)-(p-fluorophenylmethyl)hexanoyl-L-Val-L-Phe-morpholin-4-ylamide (Boc = tert-butoxycarbonyl) was prepared via peptide coupling in solution

L50 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:596036 HCAPLUS
DOCUMENT NUMBER: 125:248488
TITLE: Preparation of peptide analogs with growth hormone releasing properties.
INVENTOR(S): Lau, Jesper; Peschke, Bernd; Hansen, Thomas Kruse; Johansen, Nils Langeland; Ankersen, Michael
PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.
SOURCE: PCT Int. Appl., 252 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9622997	A1	19960801	WO 1996-DK45	19960126 <--

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE

ZA 9600544	A	19960826	ZA 1996-544	19960124 <--
CA 2211381	AA	19960801	CA 1996-2211381	19960126 <--
AU 9644315	A1	19960814	AU 1996-44315	19960126 <--
AU 705744	B2	19990603		
EP 805816	A1	19971112	EP 1996-900550	19960126 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
CN 1176645	A	19980318	CN 1996-192184	19960126 <--
BR 9606845	A	19980526	BR 1996-6845	19960126 <--
JP 11500107	T2	19990106	JP 1996-522559	19960126 <--
IL 116923	A1	20000928	IL 1996-116923	19960126 <--
PL 186511	B1	20040130	PL 1996-321590	19960126 <--
TW 482767	B	20020401	TW 1996-85102211	19960227 <--
US 6013658	A	20000111	US 1997-897239	19970717 <--
NO 9703446	A	19970926	NO 1997-3446	19970725 <--
US 6350767	B1	20020226	US 1999-443993	19991119 <--

PRIORITY APPLN. INFO.:

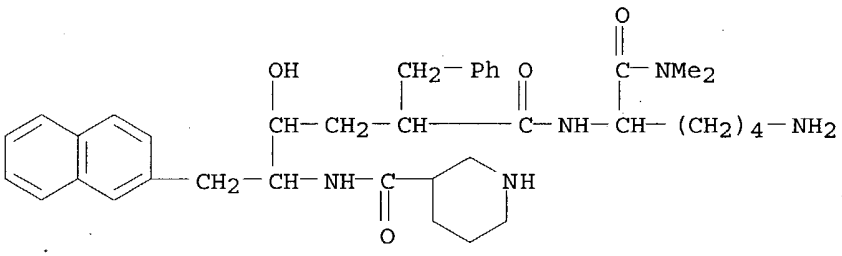
DK 1995-100	A	19950127	<--
DK 1995-99	A	19950127	<--
DK 1995-1083	A	19950928	<--
DK 1995-1084	A	19950928	<--
DK 1995-1372	A	19951204	<--
WO 1996-DK45	W	19960126	<--
US 1997-897239	A3	19970717	<--

OTHER SOURCE(S): MARPAT 125:248488

IT **181647-89-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of peptide analogs with growth hormone releasing properties)

RN 181647-89-2 HCAPLUS

CN 3-Piperidinecarboxamide, N-[5-[[5-amino-1-[(dimethylamino)carbonyl]pentyl]amino]-2-hydroxy-1-(2-naphthalenylmethyl)-5-oxo-4-(phenylmethyl)pentyl]-(9CI) (CA INDEX NAME)



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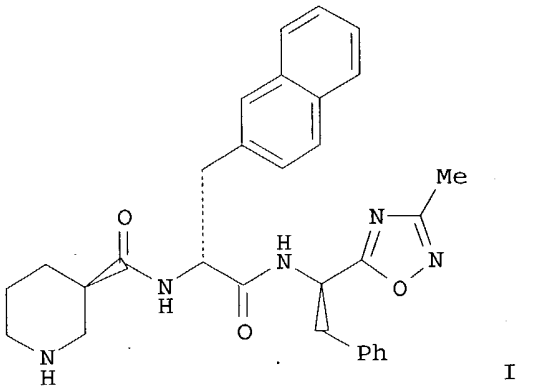

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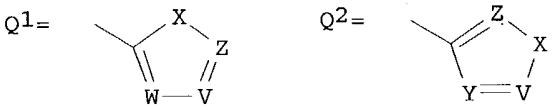


AB J(CH2)mCH(BD)ACH[(CH2)pG]FnE [n = 0, 1; m = 1, 2; p = 0-2; A = CH(OR1)CH2, CH2CO, OCH2, CH:CH, NR1W, NR1CH2; R1 = H, alkyl; W = O, S; B = CH(OR2)CH2, CH2CO, CH:CH, NR2C:W1, NR2CH2; R2 = H, alkyl; W1 = O, S; D = R5R6N(CH2)r(CR7R8)s(CH2)oCONR3CHR4, R5R6N(CH2)r(CR7R8)s(CH2)tMq(CH2)o; R3-R8 = H, (substituted) alkyl; R4R5, R6R7, R5R8, R7R8 = (CH2)iU(CH2)j; i, j = 1, 2; U = O, S, bond; M = O, S, CH:CH, (substituted) phenylene, thienylene, naphthylene, pyridylene; o, r, t = 0-4; q, s = 0, 1; r+s+t = 1-4; E = H, CHKL, Q1, Q2; L = H, OR9, CONR9R10, (substituted) alkyl, Q1, Q2; R9, R10 = H, alkyl; R9R10 = (CH2)kU1(CH2)l; k, l = 1-3; k+l = 3, 4, 6; U1 = O, S, bond; X = NR11, O, S; V = CR12, N; Y = CR13, N; Z = CR14, N; R11 = H, alkyl, aralkyl; R12-R14 = H, halo, OH, alkyl, Ph, oxazol-5-yl, etc.; K = H, R18R19Q(CH2)a(CR20R21)b(CH2)d; R18-R21 = H, (substituted) alkyl; R18R19, R18R21, R19R20, R20R21 = (CH2)k'Z(CH2)l'; k', l' = 1-3; k'+l' = 3-6; Z = O, S, bond; b = 0, 1; a, d = 0-4; a+b = 1-4; Q = CR22, N; R22 = H, alkyl; F = CH(OR23)CH2, CH2CO, NR23CW11, CH:CH, OCH2, NR23CH2; W11 = O, S; J = H, (substituted) Ph, pyridyl, naphthyl, indolyl, imidazolyl, thienyl; G = H, J], were prepared for stimulation of growth hormone release (no data). Thus, (R)-BOC-Phe-OH was refluxed with acetamide oxime and DCC in pyridine/DMF to give (R)-1-(3-methyl-1,2,4-oxadiazol-5-yl)-2-phenylethylamine. The latter was deprotected and coupled with (R)-N-BOC-3-(2-naphthyl)alanine using N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide, hydroxybenzotriazole, and Et3N in DMF. This was deprotected, coupled with (R)-N-BOC-3-piperidinecarboxylic acid, and the product was deprotected to give title compound (I).

L50 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:379679 HCAPLUS
DOCUMENT NUMBER: 125:59130
TITLE: Preparation of ethers of aspartate protease substrate isosteres as antivirals.
INVENTOR(S): Bold, Guido; Capraro, Hans-Georg; Faessler, Alexander; Lang, Marc; Bhagwat, Shripad Subray; Khanna, Satish Chandra; Lazdins, Janis Karlis; Mestan, Juergen
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 131 pp.

CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 708085	A2	19960424	EP 1995-115938	19951010 <--
EP 708085	A3	19971008		
EP 708085	B1	20020717		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 220661	E	20020815	AT 1995-115938	19951010 <--
PT 708085	T	20021129	PT 1995-115938	19951010 <--
ES 2180600	T3	20030216	ES 1995-115938	19951010 <--
AU 9534279	A1	19960502	AU 1995-34279	19951012 <--
AU 707283	B2	19990708		
FI 9504913	A	19960420	FI 1995-4913	19951016 <--
CA 2160763	AA	19960420	CA 1995-2160763	19951017 <--
BG 63042	B1	20010228	BG 1995-100067	19951017 <--
SK 282339	B6	20020107	SK 1995-1285	19951017 <--
CZ 290123	B6	20020612	CZ 1995-2713	19951017 <--
ZA 9508782	A	19960419	ZA 1995-8782	19951018 <--
NO 9504142	A	19960422	NO 1995-4142	19951018 <--
CN 1132756	A	19961009	CN 1995-120506	19951018 <--
HU 74744	A2	19970228	HU 1995-3007	19951018 <--
RU 2164229	C2	20010320	RU 1995-118112	19951018 <--
JP 08208580	A2	19960813	JP 1995-295024	19951019 <--
JP 3192070	B2	20010723		
BR 9504466	A	19970520	BR 1995-4466	19951019 <--
US 5663200	A	19970902	US 1995-545170	19951019 <--
PL 184292	B1	20020930	PL 1995-311027	19951019 <--
TW 397813	B	20000711	TW 1995-84111501	19951101 <--
US 5807891	A	19980915	US 1997-838347	19970408 <--
US 5935976	A	19990810	US 1998-138076	19980821 <--

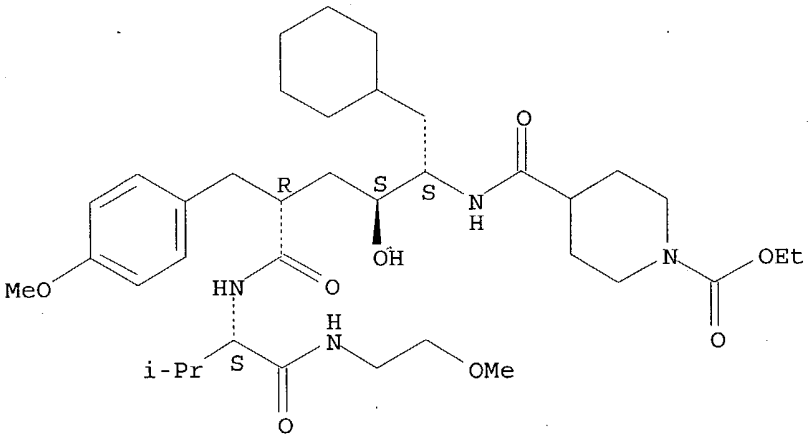
PRIORITY APPLN. INFO.:
CH 1994-3140 A 19941019 <--
CH 1995-2382 A 19950821 <--
US 1995-545170 A3 19951019 <--
US 1997-838347 A3 19970408 <--

OTHER SOURCE(S): MARPAT 125:59130

IT **178048-04-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of ethers of aspartate protease substrate isosteres as antivirals)

RN 178048-04-9 HCAPLUS
CN 1-Piperidinecarboxylic acid, 4-[3-(cyclohexylmethyl)-4-hydroxy-6-[(4-methoxyphenyl)methyl]-9-(1-methylethyl)-1,7,10-trioxo-14-oxa-2,8,11-triazapentadec-1-yl]-, ethyl ester, [3S-(3R*,4R*,6S*,9R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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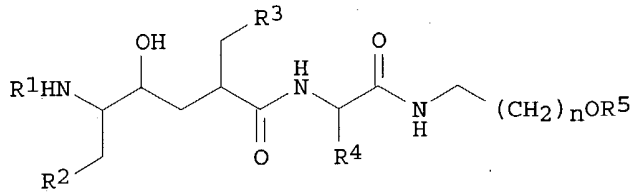

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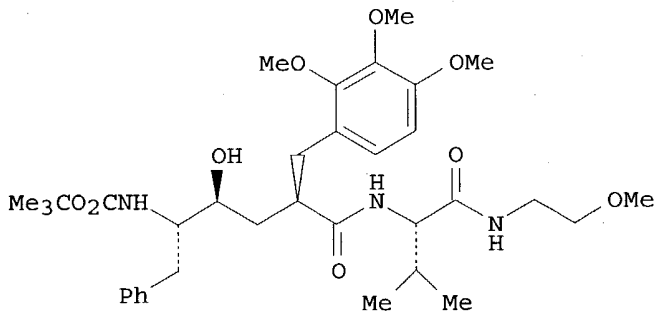


II

AB Title compds. [I; R1 = (substituted) alkoxyalkanoyl, alkoxycarbonyl, alkanoyl, arylcarbonyl, heterocyclylcarbonyl, phenylalkanoyl, arylsulfonyl, amino acid residue; R2, R3 = (substituted) cyclohexyl, cyclohexenyl, Ph, naphthyl, tetrahydronaphthyl; R4 = alkyl, cyclohexyl, Ph; R5 = alkyl; n = 1, 2; provided ≥1 salt forming group is present], were prepared Thus, title compound (II), prepared via 5(S)-[1(S)-(tert-butoxycarbonylamino)-2-phenylethyl]-3(R)-[(2,3,4-trimethoxyphenyl)methyl]dihydrofuran-2(3H)-one, at 12.5 nM combined with 12.5 nM indavir gave 76.6% inhibition of reverse transcriptase in a coculture of CEM-SS and H9/HIV-1/IIIB. Capsule formulations containing II are given.

L50 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:671728 HCAPLUS

DOCUMENT NUMBER: 119:271728
TITLE: Preparation of pseudopentapeptides with immunomodulating activity
INVENTOR(S): Degraw, Joseph I.; Almquist, Ronald; Hiebert, Charles; Smith, R. Lane; Uchida, Itsuo
PATENT ASSIGNEE(S): Japan Tobacco, Inc., Japan
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

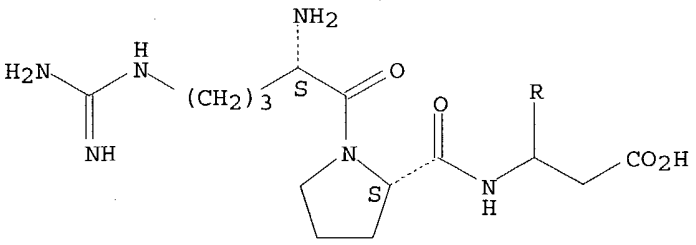
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9304080	A1	19930304	WO 1992-JP1046	19920819	<--
W: CA, JP, KR					
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE					
CA 2094822	AA	19930227	CA 1992-2094822	19920819	<--
EP 556405	A1	19930825	EP 1992-917987	19920819	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE					
JP 06501961	T2	19940303	JP 1993-504226	19920819	<--
PRIORITY APPLN. INFO.:			US 1991-749886	19910826	<--
			US 1992-920601	19920803	<--
			WO 1992-JP1046	19920819	<--

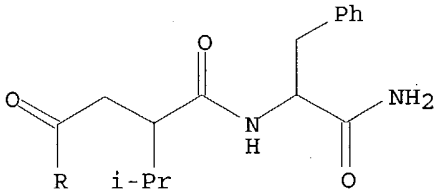
OTHER SOURCE(S): MARPAT 119:271728
IT **151011-49-3P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of, as immunomodulator)
RN 151011-49-3 HCAPLUS
CN L-Prolinamide, L-arginyl-N-[4-[[[2-amino-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]-1-(carboxymethyl)-5-methyl-2-oxohexyl]-, bis(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 151011-48-2
CMF C30 H46 N8 O7

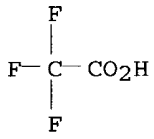
Absolute stereochemistry.





CM 2

CRN 76-05-1
CMF C2 H F3 O2



AB Thymopentin (thypentin) analogs, e.g. R-AA1-AA2-AA3-AA4-AA5-R1 [AA1 = L- or D-Arg; AA2 = optionally N-C1-6 alkylated L- or D-basic amino acid residue, a neutral/nonarom. amino acid residue, or Pro; AA3 = L- or D-Asp or Glu optionally esterified with C1-6 alkyl; AA4 = L- or D-neutral/nonarom. amino acid residue; AA5 = optionally N-C1-6 alkylated L- or D-neutral/nonarom. amino acid residue (wherein one or more H's of its aromatic portion can be substituted by NO2 or halo) or L- or D-neutral/nonpolar/large/nonarom. amino acid residue; R = C1-6 acyl, arylsulfonyl, alkylsulfonyl, arylalkylsulfonyl, alkoxycarbonyl; R1 = OH, NR2R3 (wherein R2, R3 = H, C1-6 alkyl), OR4 (R4 = C1-6 alkyl); wherein at least one of the linkages AA1-AA2, AA2-AA3, AA3-AA4, and AA4-AA5 is a modified peptide linkage selected from COCH2, CH(OH)CH2, and CH2NH and the remaining linkages are CONH or CONMe], useful for the treatment of autoimmune and infectious diseases (e.g. arthritis), are prepared Thus, coupling of a Grignard reagent PhCH2CH(CH:CH2)CH2MgBr (preparation given) with N-trityl-L-valine 2-mercaptopyridine ester (preparation given) in THF at 50-60° for 2 h followed by N-deprotection with p-MeC6H4SO3H in MeCN and N-protection with (Me3CO)2CO in CH2Cl2 containing Et3N gave N-tert-butoxycarbonyl-6-amino-7-methyl-3-benzyl-1-octen-5-one. Oxidation of the latter with RuO2.xH2O/NaIO4 in aqueous acetone gave 5-N-tert-butoxycarbonylamino-6-methyl-2-benzyl-4-oxoheptanoic acid which was bound to a Merrifield chloromethyl resin and underwent solid-phase peptide coupling with Boc-Lys(ClZ)-Asp(OcHex)-OH (ClZ = 2-chlorobenzyloxycarbonyl, cHex = cyclohexyl) (preparation given) and Boc-Arg(Tos)-OH using DCC and

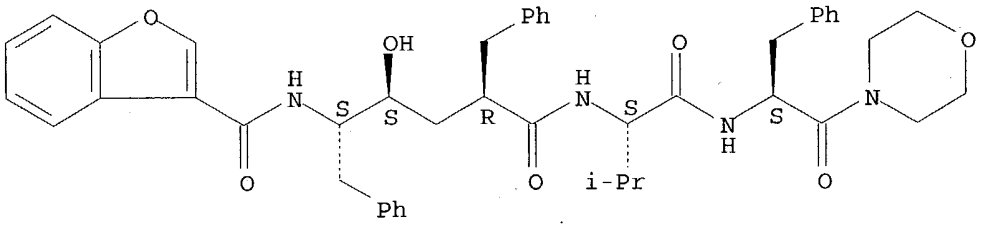
hydroxybenzotriazole to give, after deprotection and resin cleavage, H-Arg-Lys-Asp-Val(k)Phe-OH [wherein (k) indicates the linkage COCH2 as a replacement for CONH] (I). In a competitive binding assay, I at 10-3 and 10-4 M in vitro reduced the mean total count of tritiated thymopentin bound to CEM cells from 3,078 cpm (in the absence of a competitor) to 844 cpm vs. 1,150 cpm for non-radiolabeled thymopentin. The peptide analogs in vitro also increased the release of cyclic GMP in CEM cells, the production of Thy-1 antigens in spleen cells of nu/nu mice, and the serum half-life in mouse and human serum.

L50 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:650508 HCAPLUS
DOCUMENT NUMBER: 119:250508
TITLE: Preparation of 5-amino-4-hydroxyhexanoic acid derivative containing peptides as HIV protease inhibitors
INVENTOR(S): Lang, Marc; Bold, Guido; Faessler, Alexander; Schneider, Peter; Van Hoogesvest, Peter
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: Eur. Pat. Appl., 79 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 532466	A2	19930317	EP 1992-810678	19920903 <--
EP 532466	A3	19930616		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 05230095	A2	19930907	JP 1992-238424	19920907 <--
CA 2077948	AA	19930313	CA 1992-2077948	19920910 <--
AU 9222889	A1	19930318	AU 1992-22889	19920910 <--
AU 661018	B2	19950713		
IL 103126	A1	19970930	IL 1992-103126	19920910 <--
NO 9203533	A	19930315	NO 1992-3533	19920911 <--
HU 63632	A2	19930928	HU 1992-2925	19920911 <--
ZA 9206938	A	19940311	ZA 1992-6938	19920911 <--
PL 169969	B1	19960930	PL 1992-295905	19920911 <--
RU 2067585	C1	19961010	RU 1992-5052915	19920911 <--
CN 1089269	A	19940713	CN 1993-100044	19930104 <--

PRIORITY APPLN. INFO.: CH 1991-2689 A 19910912 <--
CH 1992-980 A 19920327 <--
CH 1992-2007 A 19920625 <--
OTHER SOURCE(S): MARPAT 119:250508
IT **150608-90-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(preparation of, as HIV protease inhibitor)
RN 150608-90-5 HCAPLUS
CN 3-Benzofurancarboxamide, N-[2-hydroxy-5-[[2-methyl-1-[[[2-(4-morpholinyl)-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]propyl]amino]-5-oxo-1,4-bis(phenylmethyl)pentyl]-, [1S-[1R*,2R*,4S*,5[R*(R*)]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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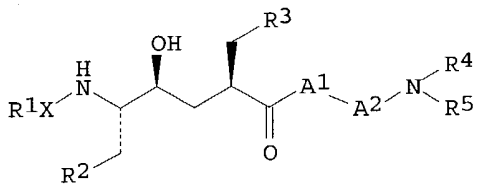

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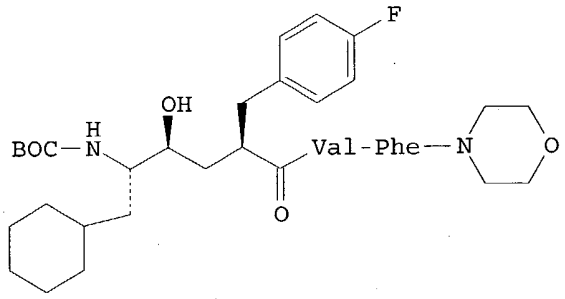


II

AB Title compds. [I; R1 = H, alkoxycarbonyl, heterocyclylcarbonyl, heterocyclyloxycarbonyl, (substituted) benzyloxycarbonyl, etc.; X = bond, α-amino acid residue; R2, R3 = (substituted) Ph, cyclohexyl; A1 = bond, α-amino acid residue; A2 = α-amino acid residue; A1A2 = dipeptide residue whose central amide bond is reduced; NR4R5 = (thio)morpholino], were prepared as HIV protease inhibitors. Thus, title compound II was prepared in many steps starting from BOC-phenylalaninal using solution phase methods. I inhibited HIV-1 multiplication in MT-2 cells with ED90's of 10-5-10-8M. Generic I oral formulations are given.

L50 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:517245 HCAPLUS
DOCUMENT NUMBER: 119:117245
TITLE: Preparation of N-imidazolylalkyl-5-amino-4-hydroxyhexanamides and analogs as retroviral protease inhibitors
INVENTOR(S): Carr, Thomas Joseph; DeMarsh, Peter Lawrence; Penwick, Ashley Edward
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**

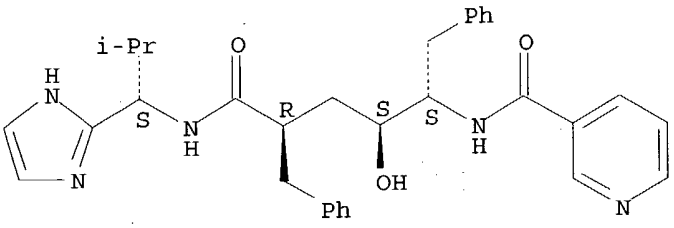
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9302057	A1	19930204	WO 1992-US6047	19920717 <--
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KR, LU, NL, NO, PL, RO, RU, SE, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9224129	A1	19930223	AU 1992-24129	19920717 <--
CN 1071434	A	19930428	CN 1992-109761	19920717 <--
ZA 9205360	A	19930614	ZA 1992-5360	19920717 <--
EP 602069	A1	19940622	EP 1992-917238	19920717 <--
R: BE, CH, DE, FR, GB, IT, LI, NL				
JP 07500577	T2	19950119	JP 1992-503016	19920717 <--
ES 2068739	B1	19951101	ES 1993-107	19930121 <--
ES 2068739	A1	19950416		

PRIORITY APPLN. INFO.: US 1991-731563 19910717 <--
US 1992-870975 19920420 <--
WO 1992-US6047 19920717 <--

OTHER SOURCE(S): MARPAT 119:117245
IT **149356-87-6P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as retroviral protease inhibitor)
RN 149356-87-6 HCAPLUS
CN 3-Pyridinecarboxamide, N-[2-hydroxy-5-[[1-(1H-imidazol-2-yl)-2-methylpropyl]amino]-5-oxo-1,4-bis(phenylmethyl)pentyl]-, [1S-[1R*,2R*,4S*,5(R*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB R5CHR1CH(OH)CHR2CHR3R4 [I; R1, R3 = fluoroalkyl, cycloalk(en)yl(alkyl), aryl(alkyl), heterocyclyl(alkyl), etc.; R2 = H, OH; R4 = azolylamino, N-(azolylalkyl)carbamoyl; R5 = substituted amino] were prepared Thus, Me2CHCHRNH2 (R = imidazol-2-yl) (preparation given) was condensed with (2R, 4S, 5S)-PhCH2CH(NHCO2CMe3)CH(OR6)CH2CH(CH2Ph)COR7 (II; R6 = SiMe2CMe3, R7 = OH) to give, after deprotection, II (R6 = H, R7 = NHCHRCHMe2, R = imidazol-2-yl). I had Ki of 1 nM to 5 μM for inhibition of HIV-1 protease.

L50 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:234486 HCAPLUS
DOCUMENT NUMBER: 118:234486
TITLE: Preparation of phosphorus containing compounds as inhibitors of retroviruses
INVENTOR(S): Hester, Jackson B.; Fisher, Jed F.; Thaisrivongs, Suvit; Maggiora, Linda Louise; Sawyer, Tomi Kim
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: PCT Int. Appl., 159 pp.

CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
WO 9217490	A1	19921015	WO 1992-US2238	19920327	<--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US					
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG					
AU 9217487	A1	19921102	AU 1992-17487	19920327	<--
EP 578745	A1	19940119	EP 1992-910121	19920327	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE					
JP 06506463	T2	19940721	JP 1992-509356	19920327	<--

PRIORITY APPLN. INFO.: US 1991-679508 19910404 <--
WO 1992-US2238 19920327 <--

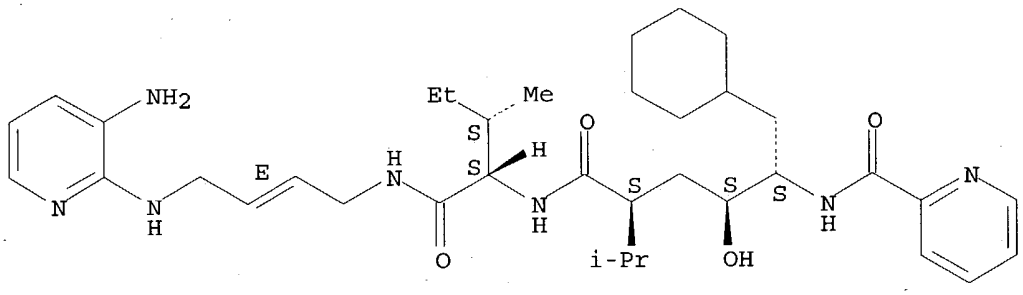
OTHER SOURCE(S): MARPAT 118:234486

IT **146363-43-1P**
RL: **SPN (Synthetic preparation); PREP (Preparation);**
SPN (Synthetic preparation); PREP (Preparation)
(preparation and HIV-1 protease inhibitory activity of)

RN 146363-43-1 HCAPLUS

CN 2-Pyridinecarboxamide, N-[4-[[[1-[[[4-[(3-amino-2-pyridinyl)amino]-2-butenyl]amino]carbonyl]-2-methylbutyl]amino]carbonyl]-1-(cyclohexylmethyl)-2-hydroxy-5-methylhexyl]-, [1S-[1R*,2R*,4R*[1R*(E),2R*]]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



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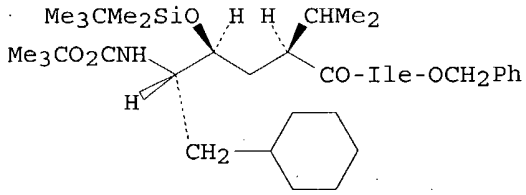

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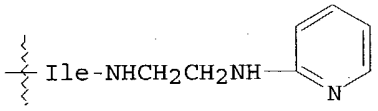
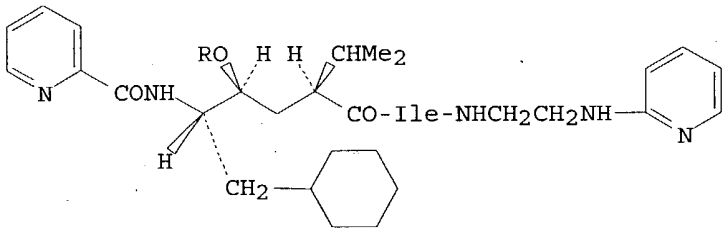


II



III

AB Phosphorus-containing peptides X-C-D-E-F-G-Z [X = H, C1-C7 alkyl, aralkyl, alkylheterocyclyl, alkylcycloalkyl, substituted acyl; C-G = independently bond, amino acid residue, dipeptide transition state analog, phosphorylated amino acid, phosphorylated dipeptide transition state analog; Z = OH, alkoxy, (substituted) amino], having at least one O-phosphate monoester or diester, parent compds. thereof, and pharmaceutically acceptable salts thereof, were prepared as inhibitors for mammalian cells infected with retroviruses. Thus, hydrogenolysis of benzyl ester I (preparation given), followed by amidation with 2-(2-aminoethylamino)pyridine gave II. Deprotection of II followed by amidation with picolinic acid gave III (R = SiMe2CMe3), which was desilylated and phosphorylated to give a title derivative III (R = PO3H2).

L50 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:572117 HCAPLUS
DOCUMENT NUMBER: 117:172117
TITLE: Inhibitors and substrates of thrombin
INVENTOR(S): Kakkar, Vijay Vir; Deadman, John Joseph; Claeson, Goran Karl; Cheng, Leifeng; Chino, Naoyashi; Elgendy, Said Mohamed Anwar; Scully, Michael Finbarr
PATENT ASSIGNEE(S): Thrombosis Research Institute, UK
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9207869	A1	19920514	WO 1991-GB1946	19911106 <--

W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU, US
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN,

GR, IT, LU, ML, MR, NL, SE, SN, TD, TG

AU 9189007	A1	19920526	AU 1991-89007	19911106 <--
AU 636521	B2	19930429		
EP 509080	A1	19921021	EP 1991-919539	19911106 <--
EP 509080	B1	20000816		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 9108805	A	19930428	ZA 1991-8805	19911106 <--
JP 05504775	T2	19930722	JP 1991-518185	19911106 <--
JP 3173786	B2	20010604		
EP 807638	A1	19971119	EP 1997-201436	19911106 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 955309	A1	19991110	EP 1999-200841	19911106 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 195531	E	20000915	AT 1991-919539	19911106 <--
ES 2149158	T3	20001101	ES 1991-919539	19911106 <--
JP 2001226397	A2	20010821	JP 2000-398079	19911106 <--
JP 3453357	B2	20031006		
US 5648338	A	19970715	US 1994-317837	19941004 <--
US 5858979	A	19990112	US 1995-459394	19950602 <--
US 6387881	B1	20020514	US 1998-205349	19981203 <--
GR 3034839	T3	20010228	GR 2000-402527	20001113 <--

PRIORITY APPLN. INFO.:

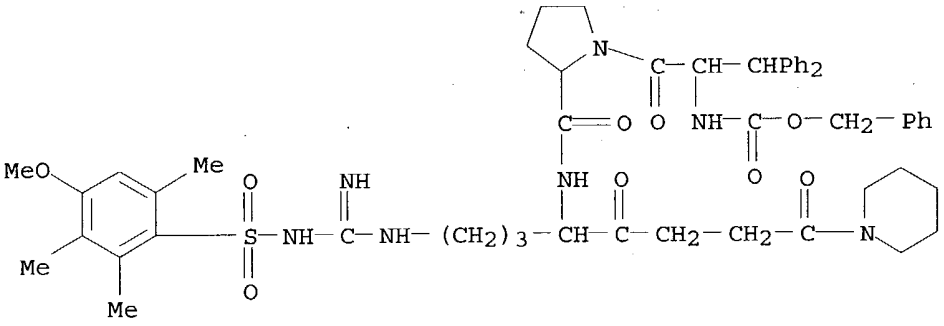
GB	1990-24129	A	19901106 <--
US	1993-158046	B1	19901106 <--
EP	1991-919539	A3	19911106 <--
JP	1991-518185	A3	19911106 <--
WO	1991-GB1946	A	19911106 <--
US	1992-866178	B1	19920919 <--
US	1994-317837	A1	19941004 <--
US	1995-459394	A1	19950602 <--

OTHER SOURCE(S): MARPAT 117:172117

IT **143290-85-1P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **SPN (Synthetic preparation)**; RACT (Reactant or reagent); **PREP (Preparation)**
(preparation and deblocking of)

RN 143290-85-1 HCAPLUS

CN L-Prolinamide, β-phenyl-N-[(phenylmethoxy)carbonyl]-D-phenylalanyl-N-[1-[3-[[imino[[(4-methoxy-2,3,6-trimethylphenyl)sulfonyl]amino]methyl]amino]propyl]-2,5-dioxo-5-(1-piperidinyl)pentyl]-, (S)- (9CI) (CA INDEX NAME)



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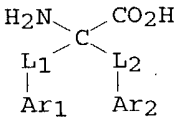


I

AB Peptides derived from D-Phe-Pro-Arg or its analogs in which the Phe is substituted by amino acids I [Ar1 and Ar2 = Ph, thienyl, pyridyl, naphthyl, thionaphthyl, indolyl; L1 and L2 = CH2, CH2CH2, OCH2, SCH2, Ar-L (Ar-L = H or benzyl in which one Ar-L can not be H when the other Ar-L means H or benzyl)] were prepared as thrombin inhibitors or substrates. Thus, AcCH(CN)CO2Et was alkylated with Ph2CHBr in the presence of KOCMe3 in tert-BuOH to give 58% Ph2CHC(CN)(NHAc)CO2Et, hydrolyzed in refluxing 20% HCl to give 81.8% DL-Ph2CH(NH2)CO2H.HCl (H-Dpa-OH.HCl). The latter was treated with PhCH2O2CCl (ZCl) in 2N NaOH to give 97% Z-DL-Dpa-OH, which was esterified with N-hydroxysuccinimide (HONSu) by DCC in 1,2-dimethoxyethane 91% Z-DL-Dpa-ONSu, which was coupled with proline in the presence of NaHCO3 in water/1,2-dimethoxyethane to give a diastereomeric mixture of Z-D-Dpa-Pro-OH and Z-L-Dpa-Pro-OH. Z-D-Dpa-Pro-OH was esterified with HONSu by DCC in dimethoxyethane to give the active ester, which was coupled with H-Arg(Mtr)-OH (Mtr = 4-methoxy-2,3,6-trimethylbenzenesulfonyl) in DMF to give 91% Z-D-Dpa-Pro-Arg(Mtr)-OH. The latter underwent the Darkin-West reaction with (MeO2CCH2CH2CO)2O in the presence of Et3N, DMAP, and pyridine to give 98% Z-D-Dpa-Pro-Arg(Mtr)-k-Gly-OMe (k means amide bond replaced by CONCH2), which was saponified and then condensed with piperidine (pip) by DCC/HONSu in dimethoxyethane to give 81% Z-D-Dpa-Pro-Arg(Mtr)-k-Gly-pip. The latter was Mtr-deblocked by CF3CO2H (TFA)/thioanisole and then Z-deblocked by hydrogenolysis to give 75% H-D-Dpa-Pro-Arg(Mtr)-k-Gly-pip.TFA. H-D-Dpa-Pro-Arg(Mtr)-k-Gly-pip inhibited thrombin in an in vitro assay with a Ki 0.2 μM.

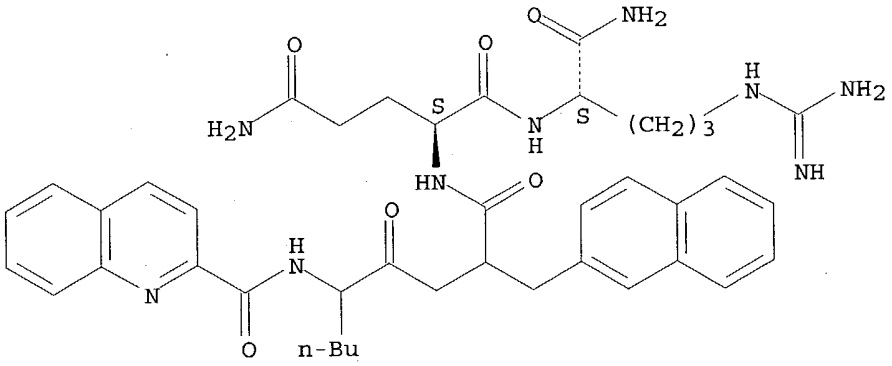
L50 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:408497 HCAPLUS
DOCUMENT NUMBER: 117:8497
TITLE: Preparation of peptide inhibitors of retroviral protease with a ketomethylene isosteric replaced amide bond
INVENTOR(S): Marshall, Garland R.; Toth, Mihaly V.
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: U.S., 6 pp. Cont.-in-part of U.S. Ser. No. 320,742.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5086165	A	19920204	US 1991-652163	19910207 <--
US 5342922	A	19940830	US 1989-320742	19890308 <--
AT 120468	E	19950415	AT 1990-870034	19900307 <--
ES 2070309	T3	19950601	ES 1990-870034	19900307 <--
CA 2060785	AA	19920808	CA 1992-2060785	19920206 <--
EP 498784	A2	19920812	EP 1992-870021	19920206 <--
EP 498784	A3	19930331		
EP 498784	B1	19970604		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, PT, SE				
JP 05065230	A2	19930319	JP 1992-21052	19920206 <--

AT 154036	E	19970615	AT 1992-870021	19920206	<--
US 6121417	A	20000919	US 1994-179052	19940107	<--
PRIORITY APPLN. INFO.:			US 1989-320742 A2	19890308	<--
			US 1991-652163 A	19910207	<--

IT **141696-73-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(preparation of, as retroviral protease inhibitor)
RN 141696-73-3 HCAPLUS
CN L-Argininamide, N2-[2-(2-naphthalenylmethyl)-1,4-dioxo-5-[(2-quinolinylcarbonyl)amino]nonyl]-L-glutaminyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Retroviral protease inhibitors containing ψ[COCH2) amide bond replacements and based on HIV protease substrates derived from HIV-1 and HIV-2 cleavage sites were prepared Thus, Qui-Thr-Ile-Nleψ[COCH2)Nal-Gln-Arg-NH2 (Qui = quinoxalic acid residue, Nal = 2-naphthylalanyl) was prepared on p-methylbenzhydrylamine resin using Boc-Nleψ[COCH2]Nal-OH prepared from BOC-Nle-OH in 5 steps. Title compds. inhibited HIV-1 protease with IC50 = 0.0046-8.08 μM.

L50 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:256051 HCAPLUS
DOCUMENT NUMBER: 116:256051
TITLE: Preparation of dipeptide isosters
INVENTOR(S): Thompson, Wayne J.; Vacca, Joseph P.; Huff, Joel R.; Lyle, Terry A.; Young, Steven D.; Hungate, Randall W.; Britcher, Susan F.; Ghosh, Arun K.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 101 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 434365	A2	19910626	EP 1990-313848	19901218	<--
EP 434365	A3	19911127			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE					
CA 2032259	AA	19910619	CA 1990-2032259	19901214	<--
FI 9006212	A	19910619	FI 1990-6212	19901217	<--

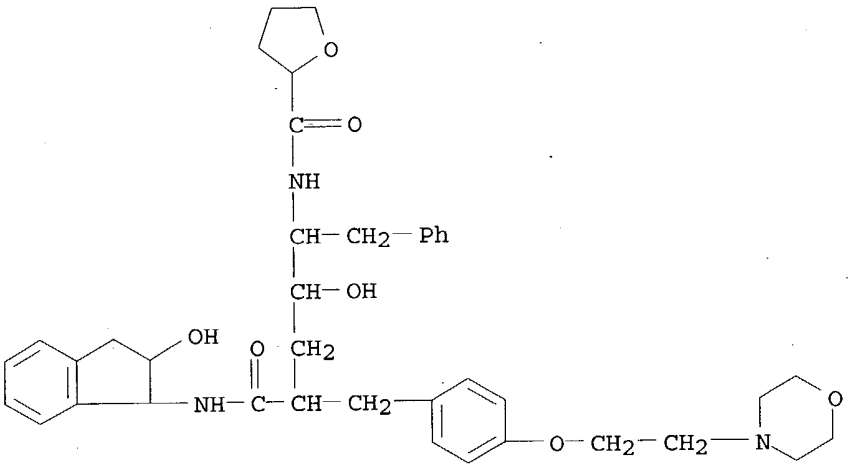
NO 9005428	A	19910619	NO 1990-5428	19901217 <--
ZA 9010125	A	19910925	ZA 1990-10125	19901217 <--
AU 9068229	A1	19910627	AU 1990-68229	19901218 <--
CN 1053607	A	19910807	CN 1990-110446	19901218 <--
JP 05345775	A2	19931227	JP 1990-419337	19901218 <--
PRIORITY APPLN. INFO.:			US 1989-452912	19891218 <--
			US 1990-597286	19901015 <--
			US 1990-619654	19901204 <--

OTHER SOURCE(S): MARPAT 116:256051

IT **138483-64-4P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as HIV inhibitor)

RN 138483-64-4 HCAPLUS

CN 2-Furancarboxamide, N-[5-[(2,3-dihydro-2-hydroxy-1H-inden-1-yl)amino]-2-hydroxy-4-[[4-[2-(4-morpholinyl)ethoxy]phenyl]methyl]-5-oxo-1-(phenylmethyl)pentyl]tetrahydro- (9CI) (CA INDEX NAME)



GI For diagram(s), see printed CA Issue.

AB A-G-B-B1-J [I; A = H, alkanoyl, alkenoyl, alkylsulfonyl, (substituted) sulfamoyl, (substituted) carbamoyl, alkylthiocarbonyl, (substituted) methoxycarbonyl; G = NHCHR9X1CHR10C(Z), NHCHR9CHR15XCO; R9, R10 = (substituted) alkyl, alkenyl, etc.; R15 = OH, (substituted) amino; Z = O, S, H2; X = (substituted) cycloalkylene; X1 = CH(OH)CH2, CH2NH, CH(NH2), etc.; B, B1 = null, NHCR21C(Z); R21 = Me2CH, CHMeEt, Ph; J = OH, alkoxy, (substituted) amino] were prepared Hexanoic acid derivative II [R1 = OH, R2 = benzyl, R4 = SiMe2CMe3] (prepared in many steps) was condensed with aminoindanol QH in DMF containing 1-hydroxybenzotriazole hydrate, ethyl[3-(dimethylamino)propyl]carbodiimide hydrochloride, and Et3N, the product treated with a mixture of citric acid, H2O, and NaHCO3, and the mixture stirred with Bu4NF in THF overnight to give II [R1 = Q, R2 = benzyl, R4 - H], which was hydrogenolyzed over Pt/C to give II [R1 = Q, R2 = R4 = H], whose condensation with N-(2-chloroethyl)morpholine in dioxane containing Cs2CO3 gave title compound II [R1 = Q, R2 = 2-morpholinoethyl, R4 = H] (III). In a study on the inhibition of the reaction of the protease expressed in Escherichia coli with a peptide substrate [H-Val-Ser-Gln-Asn-(β-naphthyl)Ala-Pro-Ile-Val-OH] III had an IC50 of 0.1-10 nM.

L50 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:591973 HCAPLUS

DOCUMENT NUMBER: 113:191973
TITLE: Preparation of peptides as peptidase inhibitors
INVENTOR(S): Bey, Philippe; Angelastro, Michael; Mehdi, Shujaath
PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals, Inc., USA
SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

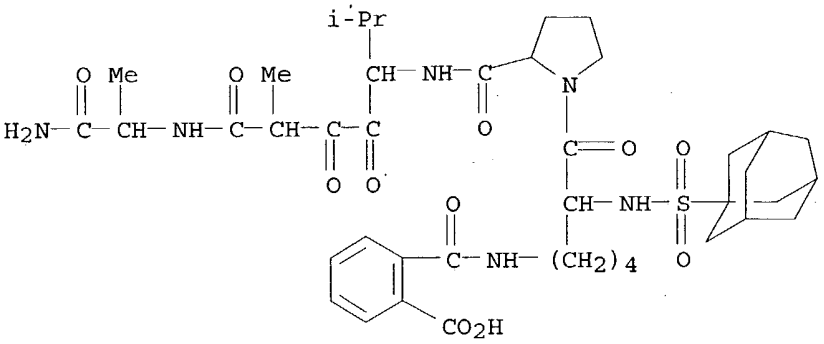
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 364344	A2	19900418	EP 1989-402763	19891006 <--
EP 364344	A3	19910911		
EP 364344	B1	19980506		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8907514	A	19900627	ZA 1989-7514	19891003 <--
ZA 8907515	A	19900627	ZA 1989-7515	19891003 <--
AU 8942491	A1	19900628	AU 1989-42491	19891004 <--
AU 617875	B2	19911205		
DK 8904946	A	19900408	DK 1989-4946	19891006 <--
DK 8904947	A	19900408	DK 1989-4947	19891006 <--
FI 8904747	A	19900408	FI 1989-4747	19891006 <--
FI 8904748	A	19900408	FI 1989-4748	19891006 <--
NO 8904013	A	19900409	NO 1989-4013	19891006 <--
NO 8904014	A	19900409	NO 1989-4014	19891006 <--
AU 8942625	A1	19900412	AU 1989-42625	19891006 <--
AU 626918	B2	19920813		
JP 02134398	A2	19900523	JP 1989-260361	19891006 <--
JP 02256654	A2	19901017	JP 1989-260360	19891006 <--
JP 3203579	B2	20010827		
HU 54105	A2	19910128	HU 1989-5247	19891006 <--
AT 153029	E	19970515	AT 1989-402762	19891006 <--
ES 2103709	T3	19971001	ES 1989-402762	19891006 <--
AT 165835	E	19980515	AT 1989-402763	19891006 <--
ES 2118710	T3	19981001	ES 1989-402763	19891006 <--
CN 1041950	A	19900509	CN 1989-107699	19891007 <--
CN 1041951	A	19900509	CN 1989-107700	19891007 <--
CA 2000340	AA	19900407	CA 1989-2000340	19891010 <--
CA 2000342	AA	19900407	CA 1989-2000342	19891010 <--
CA 2000342	C	20001003		
US 5736520	A	19980407	US 1995-434959	19950504 <--

PRIORITY APPLN. INFO.:

US	1988-254762	A	19881007 <--
US	1989-416817	B2	19891004 <--
US	1989-439201	B2	19891120 <--
US	1989-454803	B1	19891221 <--
US	1991-750439	B2	19910820 <--
US	1992-861775	B1	19920401 <--
US	1994-214991	A3	19940321 <--

OTHER SOURCE(S): MARPAT 113:191973

IT **130044-07-4P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation of, as peptidase inhibitor)
RN 130044-07-4 HCAPLUS
CN L-Prolinamide, N6-(2-carboxybenzoyl)-N2-(tricyclo[3.3.1.13,7]dec-1-ylsulfonyl)-L-lysyl-N-[5-[(2-amino-1-methyl-2-oxoethyl)amino]-4-methyl-1-(1-methylethyl)-2,3,5-trioxopentyl]- (9CI) (CA INDEX NAME)



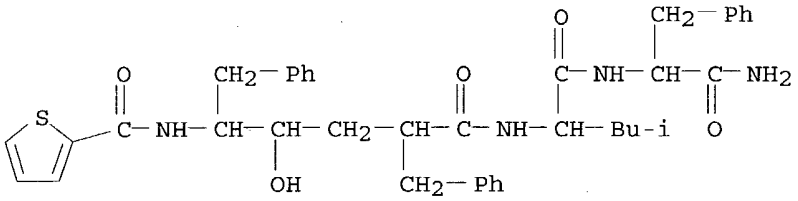
AB R1NHCHR2COX and R1NHCHR2CH(OH)X (R1 = amino-protecting group, α-amino acid, peptide comprising 2-4 α-amino acids, etc.; R2 = amino acid residue, ASiR7R8R9, C1-10 alkyl, aralkyl, aryl; A = C1-6 alkylene; X = COCHR4COR5Y; Y = NHR3, OR3; R3 = H, C1-7 alkyl, PhCH2, phenethyl; R4 = α-amino acid residue; R5 = α-amino acid, peptide comprising 2-4 α-amino acids, absent; R7, R8, R9 = C1-10 alkyl, aralkyl, aryl), their hydrates, isosteres, and pharmaceutically acceptable salts, analogs of peptidase substrates in which the N atom of the scissile amide group has been replaced by H, or a substituted malonyl moiety, were prepared as peptidase inhibitors (no data). Thus, 3,4-dioxo-5-[[(phenylmethoxy)carbonyl]amino]-6-phenylhexanoic acid (preparation given) in CH2Cl2 was treated with ClCO2CH2CHMe2 in the presence of N-methylmorpholine at -15° and the mixture was stirred 15 min. N,O-Dimethylhydroxylamine hydrochloride was added and the whole was stirred 1 h at -15°, allowed to warm to room temperature, and stirred for 3 h to give the title peptide PhCH2CH(NHCO2CH2Ph)COCOCH2CONHCH2CO2H.

L50 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:532826 HCAPLUS
DOCUMENT NUMBER: 113:132826
TITLE: Preparation of peptides as HIV protease inhibitors for treatment of AIDS
INVENTOR(S): Desolms, S. Jane; Huff, Joel R.; Vacca, Joseph P.; Sigal, Irving S.; Darke, Paul L.; Young, Steven D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 72 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 356223	A2	19900228	EP 1989-308555	19890823	<--
EP 356223	A3	19910821			
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE					
FI 8903962	A	19900225	FI 1989-3962	19890823	<--
NO 8903400	A	19900226	NO 1989-3400	19890823	<--
DK 8904141	A	19900226	DK 1989-4141	19890823	<--
ZA 8906430	A	19900530	ZA 1989-6430	19890823	<--
AU 8940192	A1	19900621	AU 1989-40192	19890823	<--
JP 02152949	A2	19900612	JP 1989-216192	19890824	<--
PRIORITY APPLN. INFO.:			US 1988-236495	19880824	<--
			US 1989-328645	19890328	<--

OTHER SOURCE(S): MARPAT 113:132826

IT **129252-78-4P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of, as AIDS protease inhibitor)
RN 129252-78-4 HCAPLUS
CN L-Phenylalaninamide, N-[4-hydroxy-1-oxo-6-phenyl-2-(phenylmethyl)-5-[(2-thienylcarbonyl)amino]hexyl]-L-leucyl-, [2R-(2R*,4S*,5S*)]- (9CI) (CA INDEX NAME)



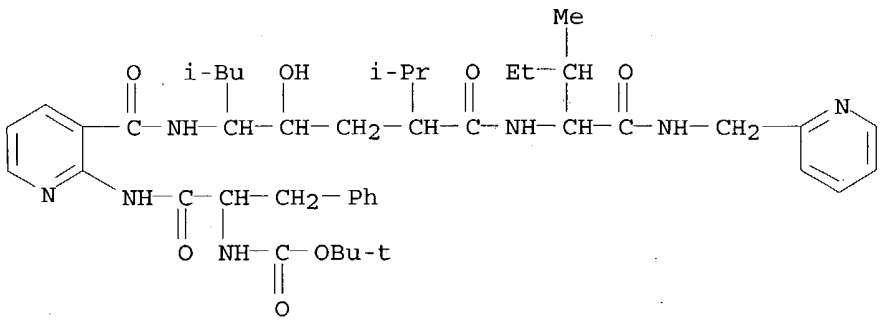
AB A-G-B1-B2-J [I; A = alkanoyl, heterocyclylcarbonyl, etc.; G = (substituted) HNCH2CH(OH)CH2CH2C(Z) and similar dipeptide isosteres; Z = O, S, NH; B1, B2 = (substituted) NHCH2C(Z) or may be absent; J = OH, (substituted) NH2, alkoxy] and their pharmaceutically acceptable salts were prepared Condensation of [[5(S)-amino-4(S)-hydroxy-6-phenyl-2(R)-(phenylmethyl)hexanoyl]leucyl]phenylalaninamide (11-step preparation given) with 2-thiophenecarboxylic acid gave I [A = thiophene-2-carbonyl, G = (5S,4S,2R)-NHCH(CH2Ph)CH(OH)CH2CH(CH2Ph)CO, B1 = Leu, B2 = Phe, J = NH2], which had an IC50 of 11 nM against synthetic HIV protease.

L50 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:36462 HCAPLUS
DOCUMENT NUMBER: 112:36462
TITLE: Preparation of renin-inhibiting angiotensinogen analogs containing nonpeptide bonds
INVENTOR(S): Ten Brink, Ruth E.
PATENT ASSIGNEE(S): Upjohn Co., USA
SOURCE: PCT Int. Appl., 91 pp.
CODEN: PIXXD2
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8901488	A1	19890223	WO 1988-US2255	19880711 <--
W: AU, DK, FI, JP, KR, NO, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8821232	A1	19890309	AU 1988-21232	19880711 <--
EP 364493	A1	19900425	EP 1988-906552	19880711 <--
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02504509	T2	19901220	JP 1988-506281	19880711 <--

PRIORITY APPLN. INFO.: US 1987-83614 19870807 <--
WO 1988-US2255 19880711 <--
OTHER SOURCE(S): MARPAT 112:36462
IT **123471-03-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(preparation of, as renin inhibitor)
RN 123471-03-4 HCAPLUS

CN Carbamic acid, [2-[[3-[[[2-hydroxy-5-methyl-1-(2-methylpropyl)-4-[[[2-methyl-1-[[(2-pyridinylmethyl)amino]carbonyl]butyl]amino]carbonyl]hexyl]amino]carbonyl]-2-pyridinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, 1,1-dimethylethyl ester, [1S-[1R*(R*),2R*,4R*(1R*,2R*)]]- (9CI) (CA INDEX NAME)



GI For diagram(s), see printed CA Issue.

AB Renin inhibitory (no data) peptides containing non-cleavable transition state inserts corresponding to the 10,11-position of angiotensinogen of the form R1Xr1(CH2)t(CO)uXv2X3CO [I; R1 = aryl, heterocyclyl, C3-7 cycloalkyl, aminoacyl, carbamoyl; X1, X2 = S, O, NH; X3 = arylene, heterocyclylene; r, u, v = 0, 1; t = 0-3], more specifically R2X6X7X8X9X10X11X12X13X14Z [II; R2 = null, H, C1-5 alkyl, acyl; X6 = null, OCH(CHR4R6)CO, NR4CH(CHR4R6)CO, etc.; X7 = null, Q1; X8X9 = I; X10X11 = Q2, Q3, etc.; X12 = null, NR4CH(CHR4R8)CO, Q4; X13, X14 = null, NR4CH(CHR4R8)CO; Z = null, (cyclic) amino, OR9; R4 = H, C1-5 alkyl, alkylaryl, heterocyclylalkyl, cycloalkylalkyl, 1- or 2-adamantyl; R5 = H, C1-5 alkyl, aryl, C3-7 cycloalkyl, heterocyclyl, C1-3 alkoxy, C1-3 alkylthio; R6 = H, Me2CH, Me2CHCH2, PhCH2, C3-7 cycloalkyl, etc; R7 = H, CHR4R10; R8 = H, C1-5 alkyl, OH, aryl, heterocyclyl, guanidinylalkyl, cycloalkylalkyl; R9 = H, C1-5 alkyl, arylalkyl, C3-7 cycloalkyl, pharmaceutically acceptable cation, etc.; R10 = R5, OH; M = CO, CH2; Q = CH2, CHOH, O, S], were prepared n-(Phenylthiomethyl)benzoic acid (preparation from m-toluic acid given) and LVA(+-BDMS)-Ile-AMP [LVA = H2NCH(CH2CHMe2)CH(OH)CH2CH(CHMe2)CO, t-BDMS = tert-butyldimethylsilyl, AMP = 2-pyridylmethylamino] in CH2Cl2 were treated with Et3N and NCP(O)(OEt)2 and the mixture was stirred 1 h to give the protected amide which was stirred with Bu4NF in THF overnight to give Q5-LVA-Ile-AMP [Q5 = n-(phenylthiomethyl)benzoyl].

L50 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:35678 HCAPLUS
DOCUMENT NUMBER: 112:35678
TITLE: Preparation of heterocyclyl nonpeptidic renin inhibitors as antihypertensives
INVENTOR(S): Rosati, Robert Louis
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: Eur. Pat. Appl., 21 pp.
CODEN: EPXXDW
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 321192	A2	19890621	EP 1988-311798	19881214 <--
EP 321192	A3	19910130		
EP 321192	B1	19931027		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 4923864	A	19900508	US 1988-261878	19881024 <--
JP 01250345	A2	19891005	JP 1988-313642	19881212 <--
JP 06092366	B4	19941116		
PL 152507	B1	19910131	PL 1988-276363	19881212 <--
CS 274671	B2	19910915	CS 1988-8203	19881212 <--
ZA 8809307	A	19900829	ZA 1988-9307	19881213 <--
CA 1314545	A1	19930316	CA 1988-585722	19881213 <--
HU 48277	A2	19890529	HU 1988-6423	19881214 <--
HU 201564	B	19901128		
AU 8826881	A1	19890615	AU 1988-26881	19881214 <--
AU 593181	B2	19900201		
FI 8805783	A	19890616	FI 1988-5783	19881214 <--
FI 88295	B	19930115		
FI 88295	C	19930426		
NO 8805549	A	19890616	NO 1988-5549	19881214 <--
NO 172935	B	19930621		
NO 172935	C	19930929		
CN 1034366	A	19890802	CN 1988-108575	19881214 <--
CN 1025676	B	19940817		
DK 8806948	A	19890811	DK 1988-6948	19881214 <--
DD 283381	A5	19901010	DD 1988-323142	19881214 <--
SU 1651786	A3	19910523	SU 1988-4613032	19881214 <--
AT 96433	E	19931115	AT 1988-311798	19881214 <--
ES 2059540	T3	19941116	ES 1988-311798	19881214 <--
PRIORITY APPLN. INFO.:			US 1987-132373	19871215 <--
			EP 1988-311798	19881214 <--

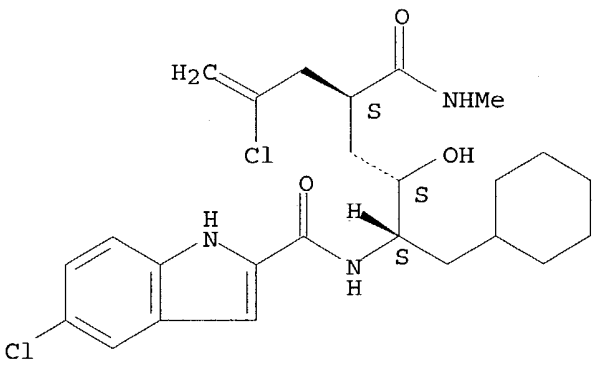
OTHER SOURCE(S): CASREACT 112:35678; MARPAT 112:35678

IT **124184-82-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; THU (Therapeutic use); BIOL (Biological study); **PREP (Preparation)**; USES (Uses)
(preparation of, as antihypertensive)

RN 124184-82-3 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[6-chloro-1-(cyclohexylmethyl)-2-hydroxy-4-[(methylamino)carbonyl]-6-heptenyl]-, [1S-(1R*,2R*,4R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB HET-CONHCHR1CH(OH)CH2CHR2CONHR3 [I; HET = hydroquinolinyl, imidazopyridyl,

hydroxyquinoxalinyl, dichloropyrrolyl, pyrrolopyridyl, (un)substituted indolyl; R1 = C6-8 cycloalkyl, Me2CH; R2 = C3-5 alkyl, Ph, MeCH:CH, Me2C:CH, halovinyl,hydroxy C1-3 alkyl, amino C1-4 alkyl; R3 = C1-6 alkyl, morpholinoethyl] and their pharmaceutically acceptable salts, useful as antihypertensives (no data) were prepared (2R,4S,5S)-6-Cyclohexyl-5-amino-2-(2'-chloro-2'-propenyl)-γ-hexanolactone hydrochloride (165.5 mg) was coupled with 97.8 mg 5-chloroindole-2-carboxylic acid in the presence of N-methylmorpholine, N-hydroxybenzotriazole and dicyclohexylcarbodiimide in CH2Cl2 to give 226 mg (2R,4S,5S)-I (HET = 5-chloroindol-2-yl; R1 = cyclohexyl; R2 = ClC:CH2; R3 = Me).

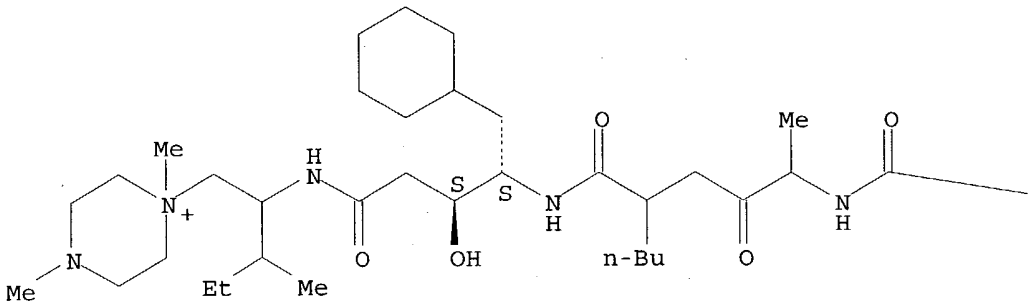
L50 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:407784 HCAPLUS
DOCUMENT NUMBER: 111:7784
TITLE: Preparation of peptides containing statine or other peptide bond isosteres of phenylalanylhistidine as renin inhibitors
INVENTOR(S): Greenlee, William J.; Parsons, William H.; Patchett, Arthur A.; Chakraverty, Prasun K.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Jpn. Kokai Tokkyo Koho, 60 pp.
CODEN: JKXXAF
DOCUMENT TYPE: **Patent**
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63146850	A2	19880618	JP 1987-284387	19871112 <--
EP 278158	A2	19880817	EP 1987-309687	19871102 <--
EP 278158	A3	19900523		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
DK 8705909	A	19880513	DK 1987-5909	19871111 <--

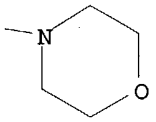
PRIORITY APPLN. INFO.: US 1986-929464 19861112 <--
OTHER SOURCE(S): MARPAT 111:7784
IT **119806-92-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **SPN (Synthetic preparation)**; BIOL (Biological study); **PREP (Preparation)**
(preparation of, as renin inhibitor)
RN 119806-92-7 HCAPLUS
CN Piperazinium, 1-[2-[[4-[[2-butyl-5-[(4-morpholinylcarbonyl)amino]-1,4-dioxohexyl]amino]-5-cyclohexyl-2,4,5-trideoxy-L-threo-pentonoyl]amino]-3-methylpentyl]-1,4-dimethyl-, chloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



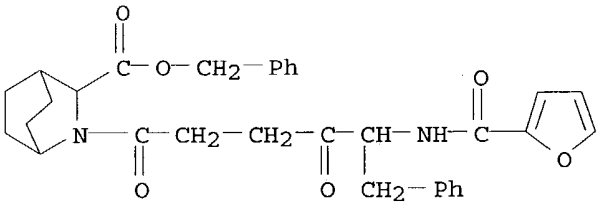
AB The title peptides A-B-NR2CH[(CH2)nR3]E [I; A = R1(CH2)mCH[(CH2)nR]SO2 or groups represented by 5 other Markush structures; R, R1 = H, aryl, C1-4 alkyl, OH, SH, (mono- or dialkyl)amino, CO2H, C1-4 alkoxylcarbonyl; aryl = (mono-, di-, or tri-substituted) Ph, naphthyl; m, n = 0-3; R2 = H, C1-4 alkyl; R3 = CHR4R5; when R5 = H, R4 = H, C1-5 alkyl, aryl, het, C1-3 alkoxy, C1-3 alkylthio, (mono- or disubstituted) C3-7 cycloalkyl; het = (benzo-fused), (mono- or disubstituted), 5- to 7-membered heterocyclyl; when R4 = C1-4 hydroxyalkyl or C1-4 aminoalkyl, R5 = H or C1-3 alkyl; B = KCH[(CH2)nR6]CO or bivalent groups represented by 2 other Markush structures; K = NR1, CH2; R6 = (mono-substituted) C1-4 alkyl, aryl, Het; E = CH(W)-G; W = OH, NH2, C1-4 alkanoyloxy, C1-4 alkanoyloxy-C1-4 alkyl; G = Q-CO-T-V; Q = bond, (un)substituted CH2, CH2CH2; T = bond, substituted NHCH2CO; V = OH, (un)substituted alkoxy, etc.] were prepared as renin inhibitors. Treatment of Nα-tert-butoxycarbonyl-L-histidyl-(3S,4S)-4-amino-5-cyclohexyl-3-hydroxypentanoyl hydrazide with isoamyl nitrite in THF and peptide coupling of the resulting acyl azide with 3(S)-aminoquinuclidine-2HCl in the presence of Et3N gave 80% Nα-tert-butoxycarbonyl-L-histidyl-(3S,4S)-4-amino-5-cyclobutyl-3-hydroxypentanoyl-3-quinuclidinylamide. Deprotection of the latter with 50% CF3CO2H/CH2Cl2, followed by amidation with 3-benzyl-2(S)-(isopropylsulfonylmethyl)propionic acid N-hydroxysuccinimide ester, gave 3-benzyl-2(S)-(isopropylsulfonylmethyl)propionyl-L-histidyl-(3S,4S)-4-amino-5-cyclohexyl-3-hydroxypentanoyl-3-quinuclidinylamide (II). II

inhibited renin with an IC50 of 11 nM.

L50 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1986:34337 HCAPLUS
DOCUMENT NUMBER: 104:34337
TITLE: Diamide derivatives of azabicycloalkanes and pharmaceutical compositions containing them
INVENTOR(S): Vincent, Michel; Remond, Georges; Laubie, Michel
PATENT ASSIGNEE(S): ADIR, Fr.
SOURCE: Fr. Demande, 27 pp.
CODEN: FRXXBL
DOCUMENT TYPE: **Patent**
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 2554446	A1	19850510	FR 1983-17519	19831104 <--
FR 2554446	B1	19861128		

PRIORITY APPLN. INFO.: FR 1983-17519 19831104 <--
OTHER SOURCE(S): CASREACT 104:34337
IT **99697-06-0P**
RL: RCT (Reactant); **SPN (Synthetic preparation)**; **SPN (Synthetic preparation)**; RACT (Reactant or reagent); **PREP (Preparation)**
(preparation and hydrogenolysis of)
RN 99697-06-0 HCAPLUS
CN 2-Azabicyclo[2.2.2]octane-3-carboxylic acid, 2-[5-[(2-furanylcarbonyl)amino]-1,4-dioxo-6-phenylhexyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



GI For diagram(s), see printed CA Issue.
AB Amides I (Q forms and azabicycloalkane system; R1 = H, alkyl; R2 = alkyl, phenylalkyl, thienyl-, furyl-, tetrahydrofuryl-, or pyridylalkyl; R3 = Ph, halo- or sulfamoylphenyl, thienyl, furyl, tetrahydrofuryl, pyridyl) were prepared as antihypertensives. Thus, tert-Bu octahydroindole-2-carboxylate was condensed with Me2CHCH2CH(NHBz)COCH2CH2CO2H by DCC/1-hydroxybenzotriazole to give octahydroindole derivative II (R4 = CMe3), which was de-tert-butylated by HCl/EtOAc to give II (R4 = H).

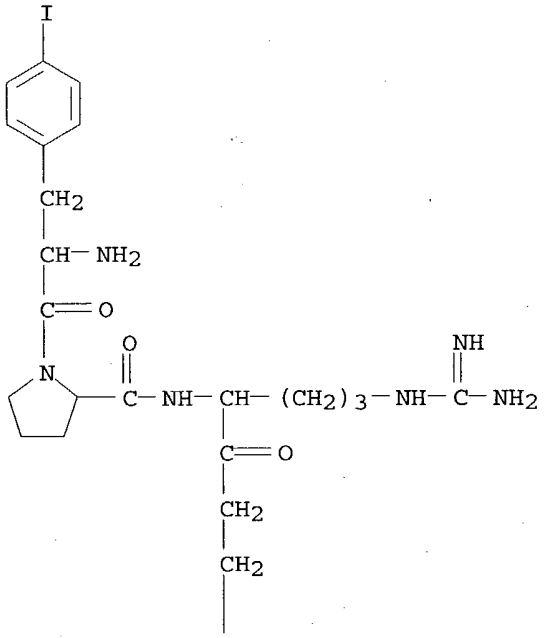
L50 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:185498 HCAPLUS
DOCUMENT NUMBER: 102:185498
TITLE: Peptide analogs and their use in enzyme inhibition
INVENTOR(S): Szelke, Michael; Jones, David Michael
PATENT ASSIGNEE(S): UK
SOURCE: Eur. Pat. Appl., 49 pp.
CODEN: EPXXDW

DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

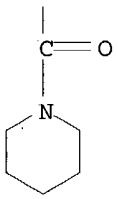
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
EP 118280	A1	19840912	EP 1984-301297	19840228	<--
EP 118280	B1	19890712			
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
WO 8403507	A1	19840913	WO 1984-GB63	19840228	<--
W: AU, DK, FI, JP, NO, US					
AU 8426516	A1	19840928	AU 1984-26516	19840228	<--
AU 596783	B2	19900517			
JP 60500870	T2	19850606	JP 1984-501509	19840228	<--
AT 44533	E	19890715	AT 1984-301297	19840228	<--
CA 1322078	A1	19930907	CA 1984-448562	19840229	<--
ES 530262	A1	19851201	ES 1984-530262	19840302	<--
FI 88398	B	19930129	FI 1984-4230	19841029	<--
FI 88398	C	19930510			
US 4638047	A	19870120	US 1984-668277	19841031	<--
DK 8405202	A	19841101	DK 1984-5202	19841101	<--
NO 8404395	A	19841105	NO 1984-4395	19841105	<--
NO 167809	B	19910902			
NO 167809	C	19911218			
US 4772686	A	19880920	US 1987-1851	19870109	<--
PRIORITY APPLN. INFO.:			GB 1983-5985	19830304	<--
			EP 1984-301297	19840228	<--
			WO 1984-GB63	19840228	<--

IT **95198-97-3P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**
(preparation of)
RN 95198-97-3 HCAPLUS
CN L-Prolinamide, 4-iodophenylalanyl-N-[1-[3-[(aminoiminomethyl)amino]propyl]-2,5-dioxo-5-(1-piperidinyl)pentyl]- (9CI) (CA INDEX NAME)

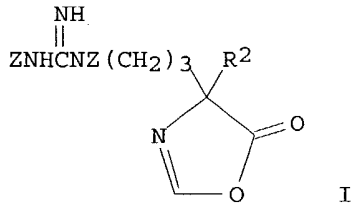
PAGE 1-A



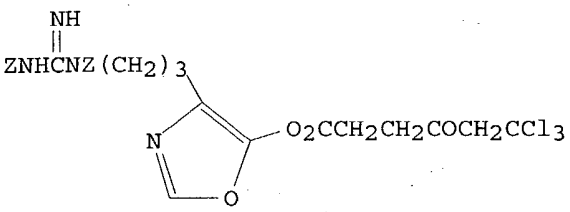
PAGE 2-A



GI



I



II

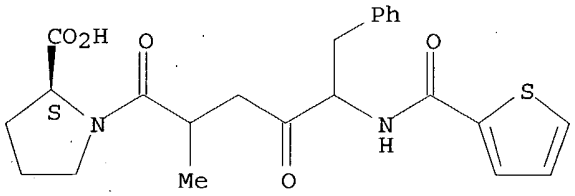
AB Fibrinogen sequence 14-20 analogs R-X-X1-X2-Pro-Arg-X3-R1 [R, R1 = terminal groups optionally including further amino acid residues; X = Gly, Phe, or other lipophilic amino acid residues; X1 = Gly, MeAla, Val, Pro, or ring homolog of Pro; X2 = hydroxy-reduced or oxo dipeptide residue in which the 1st residue is Arg or has an amidino side chain and the 2nd residue is Gly, Ala, or related residue with a hydrocarbon side chain optionally terminated by OH; X3 = Val, Pro, NH(CH2)nCO (n = 0-5)] were prepared as antithrombotics due to their ability to inhibit thrombin. Thus, H-Arg(Z2)-OH (Z = CO2CH2Ph) was cyclized by DPECI.HCl (N-dimethylaminopropyl-N'-ethylcarbodiimide hydrochloride) in THF containing Et3N to give oxazolone I (R2 = H), which was acylated with ClCOCH2CH2COCH2CCl3 to give oxazole II, which underwent rearrangement to I (R2 = COCH2CH2CO2CH2Cl3), which was cleaved by pyridine/HOAc and then deesterified by Zn/Na2H2PO4 in THF to give HCO-DL-Arg(Z2)-Gly-OH (III). Boc-Pro-Arg(Z2)-Val-NHEt (Boc = Me3CO2C) was Boc-deblocked and then coupled with III via the pentafluorophenyl (Pfp) active ester to give HCO-Arg(Z2)-Gly-Pro-Arg(Z2)-Val-NHEt, which was deformylated and then coupled with Boc-D-Phe-Pro-OPfp to give Boc-D-Phe-Pro-X4-Gly-Pro-Arg(Z2)-Val-NHEt [IV; X4 = DL-Arg(Z2)], which were separated into IV [X4 = D-Arg(Z2)] and IV [X4 = L-Arg(Z2)] (V). V was Z-deblocked by hydrogenolysis to give R3-D-Phe-Pro-Arg-Gly-Pro-Arg-Val-NHEt (VI, R3 = Boc), which was Boc-deblocked by 2N HCl to give VI (R3 = H) (VII). The Ki of VII for human thrombin was 3 μM.

L50 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1983:505698 HCAPLUS
DOCUMENT NUMBER: 99:105698
TITLE: Amide derivatives
INVENTOR(S): Davies, David Huw; Preston, John; Walker, Edward Raymond Halstead; Ratcliffe, Arnold Harry
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: S. African, 43 pp.
CODEN: SFXXAB
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

ZA 8108206 A 19821027 ZA 1981-8206 19811125 <--
PRIORITY APPLN. INFO.: ZA 1981-8206 19811125 <--
IT **86157-35-9P**
RL: **SPN (Synthetic preparation)**; **PREP (Preparation)**; **PREP (Preparation)**; RACT (Reactant or reagent)
(preparation and esterification of, with methanol)
RN 86157-35-9 HCAPLUS
CN L-Proline, 1-[2-methyl-1,4-dioxo-6-phenyl-5-[(2-thienylcarbonyl)amino]hexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB R-X-NR1CHR2-X1-CHR3CHR4CONR5CR6R7-X2-R8 [R = H, (un)substituted alkyl, aryl, aryloxy, alkoxy, aralkoxy, haloalkyl, alkenyl, haloalkenyl, cycloalkyl, R9CONHCHR10 (R9 = alkyl, cycloalkyl, aryl, R10 = H, alkyl, aralkyl), heterocyclic group; R1 = H, alkyl, aralkyl, aryl; R2 = alkyl, alkenyl, aralkyl, aralkenyl, aryl, indolylmethyl, heterocyclic-substituted alkyl; R3 = H, alkyl; R4 = H, alkyl, aralkyl; R5 = H, aryl, alkyl, aralkyl; R6 = H, aryl, heterocyclic group, alkyl, hydroxyalkyl, aralkyl, heterocyclic-substituted alkyl; R5R6 = hydroxy or oxo substituted alkylene or alkenylene, oxa, thio, or aza derivative of alkylene or alkenylene; R7 = H, alkyl; C6R6 = alkylene; R8 = OH, (un)substituted alkoxy, (un)substituted NH2, aryloxy, arylthio; R10 = O joined to the terminal C atom of R6 when it is alkyl; X = CO, CS, SO2, NHCO; X1 = CO, CH(OH), CS, C(:NOR11) (R11 = H, alkyl, aralkyl); X2 = CO, CH2] were prepared as antihypertensives (no data) due to their ability to inhibit angiotensin-converting enzyme. Thus, 2-thenoic acid was treated with SOCl2 to give the acid chloride, which was condensed with N-[(RS)-5-amino-(RS)-2-methyl-4-oxo-6-phenylhexanoyl]-L-proline to give N-[(RS)-2-methyl-4-oxo-6-phenyl-(RS)-5-(2-thenoylamino)hexanoyl]-L-proline.

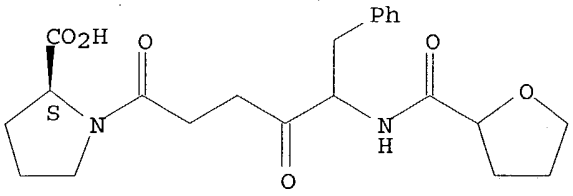
L50 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1982:545276 HCAPLUS
DOCUMENT NUMBER: 97:145276
TITLE: Oxoalkanoic acid derivatives as inhibitors of angiotensin converting enzyme
INVENTOR(S): Almquist, Ronald G.; De Graw, Joseph I.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 11 pp. Cont.-in-part of U.S. Ser. No. 44,685, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: **Patent**
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4329473	A	19820511	US 1980-219885	19801224 <--

PRIORITY APPLN. INFO.: US 1979-44685 19790601 <--
OTHER SOURCE(S): CASREACT 97:145276

IT **77921-62-1P**
RL: **SPN (Synthetic preparation); PREP (Preparation)**
(preparation and angiotensin-converting enzyme-inhibiting activity of)
RN 77921-62-1 HCAPLUS
CN L-Proline, 1-[1,4-dioxo-6-phenyl-5-[[(tetrahydro-2-furanyl)carbonyl]amino]hexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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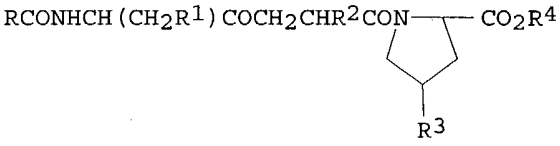
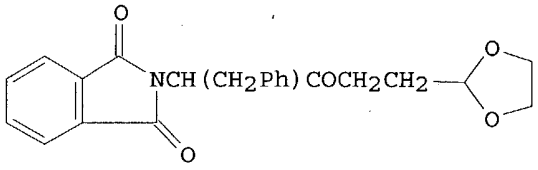
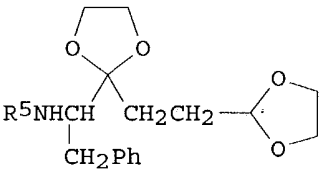


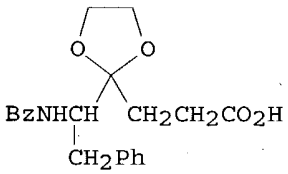
I



II



III



IV

AB Proline derivs. I (R = aryl, alkyl, alkoxy; R1 = aryl; R2 = H, alkyl; R3 = H, OH; R4 = H, alkyl) were prepared as antihypertensives due to their ability to inhibit angiotensin-converting enzyme (ACE). Thus, N-phthaloyl-L-phenylalanine was treated with PCl5 in benzene to give the acid chloride, which was esterified with 2-mercaptopyridine to give the thio ester (88%), which was treated with 2-(2-bromoethyl)-1,3-dioxolane and Mg in THF at 30-5° to give 35% ketone II. II was treated with HOCH2CH2OH to give the cyclic ketal (58%), which was deblocked by hydrazinolysis to give amino ketal III (R5 = H), which was benzoylated with BzCl to give 73% III (R5 = Bz). The latter was oxidized by CrO3 to give acid IV, which underwent deketalization to give 74% BzNHCH(CH2Ph)COCH2CH2CO2H, which was condensed with H-Pro-OCH2Ph by DCC/1-hydroxybenzotriazole in CH2Cl2 to give 71% BzNHCH(CH2Ph)COCH2CH2CO-Pro-OCH2Ph, which was debenzylated by hydrogenolysis to give 72%

BzNHCH(CH2Ph)COCH2CH2CO-Pro-OH (V). V inhibited ACE with an ID50 of 3.2 mM.

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